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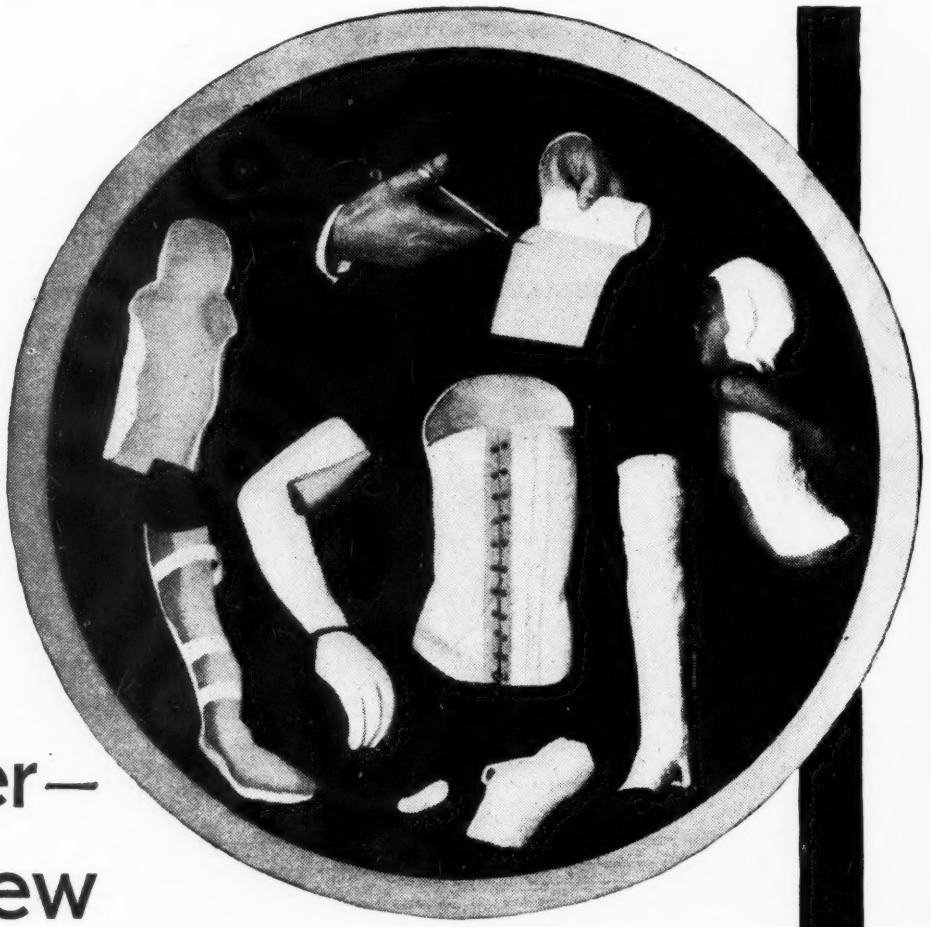

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ON

THE OUTLOOK OF RESEARCH IN THERAPEUTICS*

BY

J. A. GUNN, M.D., D.Sc., F.R.C.P.

PROFESSOR OF PHARMACOLOGY IN THE UNIVERSITY OF OXFORD

Research in therapeutics can for convenience be considered from three angles—experimental pharmacology, chemotherapy, and experimental therapeutics—and, in the case of new drugs, investigation generally follows this logical sequence. This has not been, however, in the case of a large proportion of the drugs which are still in use, the historical order. It has been computed that about 50 per cent. of the drugs in our present *Pharmacopoeia* were in use by the Arabic-speaking physicians of the Middle Ages. Many others, like cinchona and ipecacuanha, came to us early from the New World. All these had been first tested by direct observation of their effects on disease in man.

Modern medicine acquired an unwieldy heritage of drugs so introduced. When the new science of experimental pharmacology began, roughly about a century ago, it was confronted with the Augean task of purging the materia medica of an accumulation of inactive and useless drugs. Experimental pharmacology at first led, not to an increase, but to a decrease in the number of remedies in use. What frequently happened was that a reputed remedy, when examined pharmacologically, failed to display such actions as could explain its therapeutic use. This led to a reinvestigation of its therapeutic claims, which were often proved to be ill founded, and it was eventually discarded. It must be admitted, however, that in this process of elimination pharmacology made many mistakes.

Financial Aspect of Therapeutic Errors

Drugs cost money, and a drug which fails to produce a certain effect is a dead economic loss. Apart from patent medicines—on which something like £2,500,000 is spent in a single year by consumers in this country—the amount of money spent on useless drugs, and on drugs that, from inactivity, inappropriateness, or incorrect dosage, fail to produce any remedial effect, must run into millions of pounds every year. To take one example: sarsaparilla was rejected from the *British Pharmacopoeia* of 1914, almost exactly 250 years after its introduction into European medicine. Yet nearly a hundred years ago Christison wrote as follows:

> "The probability is much in favour of the drug turning out very inferior in virtue to what its admirers imagine. The question is not unimportant. Admitting sarsaparilla does no harm, the subject deserves consideration in an economical point of view. In 1831 the quantity consumed in Britain amounted to 107,000 pounds (Pereira); and in 1821, the apothecary of one of the great London hospitals informed me that he had paid at that time £1,500 for a single year's consumption of it."

In the year 1870 the importation of sarsaparilla into the United Kingdom amounted to 345,000 lb., valued at over £26,000. If we can take the year 1870, which happens to be the only year for which I could find actual figures, and we add to the cost of the crude drug as imported the manufacturers' cost of making galenical preparations, the retail druggist's cost of dispensing, together with the cost of transport, etc., it is probably a conservative estimate that the consumer in this country spent in that year £50,000 for sarsaparilla alone. In other words, an amount of money was spent in a year on sarsaparilla which would at that time have sufficed to build and equip an institute of therapeutics and endow the salary of a director.

The questions we have to ask ourselves is whether this process of elimination of useless drugs has proceeded with reasonable speed; whether, if only from the point of view of economy, there has ever been any deliberate and concerted plan to rid medicine of the incubus of spurious remedies. The answer to this question is—No!

Tardiness of Therapeutic Advance

It is not only in the discarding of useless preparations that the art of therapeutics has been hesitant. The positive recognition of those with well-substantiated claims was often equally tardy. More than 100 years ago, Quincy, who was not given to exaggerated statements, extolled ipecacuanha as the divine remedy for dysentery; but it was only about twenty years ago when it was decided that its merit lay in the alkaloidal, rather than in the tannin, content of the drug.

When the remedial value of a drug was beyond dispute one might have thought that the determination of the optimum quantity to be administered in a particular disease would have been a relatively simple matter. But this anticipation is not in accord with historical facts. Quinine, as distinct from the preparations of cinchona, has been used in the treatment of malaria for about a century. As long ago as 1842 Christison wrote as follows in regard to its dosage.

> "From twelve to eighteen grains divided into four or six doses will be generally sufficient for the ordinary intermittents of Europe; but the severe forms which occur in the south of Europe, and still more those of the Tropics, require thirty-six or forty grains on an average; and in Madagascar Dr. Allan informs me he had not infrequently to use ninety grains divided into three doses."

If the knowledge of quinine had reached that stage of precision in 1842, one would have thought that by 1912 there would be nothing further to learn about its dosage in malaria. But during the war it was necessary to institute special experiments to decide what was the optimum dosage to prevent relapses in malaria. Every administration of a drug may be regarded as an experiment, and the administration of quinine in malaria has been one of the most gigantic biological experiments ever made. Can anyone believe that anything near the maximum amount of information has been obtained from this colossal experiment?

Neglect of Therapeutics

So far as the last half century is concerned, one reason for this delay and uncertainty in estimating the value of reputed remedies is not far to seek. It was simply neglect of, and some lack of interest in, therapeutics. It has been an era during which enormous advances have been made in the pathology of diseases. Contemporaneously there were rapid developments in the recognition of distinct diseases. It was pardonable that during this period the question of the treatment of disease should receive less attention, because it was realized that rational therapy depended, first of all, upon accurate identification of the disease, and, secondly, upon a knowledge of the pathological conditions to be treated. In an address delivered fifty years ago at the opening of the Section of Pathology of this Association at Worcester, Hughlings Jackson began with these sentences:

> "Pathology is the basis of every rational system of therapeutics. . . . That, possibly, the greater part of our most effectual treatment is at present empirical I would not deny, but that therapeutics will become rational is what we all hope. . . . It is evident that, for rational therapeutics, we must know what is to be treated."

[3738]

* Made in opening a discussion in the Section of Pharmacology and Therapeutics at the Centenary Meeting of the British Medical Association, London, 1932.

It was in fact recognized at that time that the first step towards rational therapy was a knowledge of the disease to be treated, and it was logical and inevitable that research should first occupy itself with that necessary precedent.

About the beginning of this century, however, murmurings began to be heard that, both in teaching and in investigation, the treatment of disease was unduly neglected. The object of this discussion is to take stock of the present position and to inquire, without recriminating the past, but merely benefiting from its experience, whether everything is being done that ought to be done to remedy this alleged, and probably actual, neglect of therapeutics.

Prospects of Therapeutic Research

I propose therefore, so far as time will allow, to cast a glance at the prospects of therapeutic research at the present time and especially in this country, and for this purpose to adopt the convenient classification of therapeutics into experimental pharmacology, chemotherapy, and, finally, the treatment of disease in man.

Experimental Pharmacology

Pharmacological research presupposes a general knowledge of physiology and of physiological methods. It is in many ways inseparable from pure physiology. For example, adrenaline, being a normal hormone of the body, may justly belong to pure physiology, but ephedrine, a natural plant alkaloid closely resembling adrenaline in chemical composition and in physiological action, belongs rather to the domain of pharmacology.

This close contact or overlapping of physiology and pharmacology at certain points has led some to believe that pharmacology can be adequately regarded and treated as a mere apanage of physiology. This, I think, is a mistake. In the first place, the tendency is for physiological research to become more specialized, but the bulk of the pharmacological research can never become specialized. In the investigation, for example, of new compounds as potential remedies the investigator must run the gamut, as far as possible, of all their physiological actions, at least within the limits of " therapeutic " doses. Consequently, the majority of pharmacologists must possess a wide training in physiological technique, and I think it is fair to say that the tendency at the present time is for the pharmacologist to have to acquire a wider personal experience of physiological methods than is possessed by the majority of physiologists themselves. Secondly, the literature of pharmacology is so vast that no one man can hope to cover it all. *A fortiori* he cannot hope to grapple with the still greater literature of pure physiology as well. Thirdly, unless pharmacology is to become a sterile and detached subject, the professed pharmacologist must, both in the interests of teaching medical students and of research, maintain a knowledge of the use of drugs in diseases and therefore of the diseases themselves. For these reasons, among others, pharmacology makes full demands upon a man's time and energies. In the future it will become less and less possible for one man to be both a physiologist and a pharmacologist. If this is so, and pharmacologists are necessary, there must be careers open to them.

At no period has treatment by means of drugs been on so sure a foundation or so amply justified. In spite of the apathy towards pharmacology in this country at the moment, it is quite certain that it will become an increasingly important branch of medicine. I should therefore like to take this opportunity to urge medical schools to make adequate and sympathetic provision for teaching and research in experimental pharmacology.

Chemotherapy

According to strict definition, pharmacology is concerned with the physiological action of drugs, and is consequently more often a basis for the relief of symptoms than for the cure of disease. For example, such important drugs as digitalis, pituitrin, adrenaline, anaesthetics, hypnotics, etc., do not remove the underlying causes of disease. They may, however, sometimes relieve symptoms to the extent of removing disability, and so may be looked upon as curative. It is chiefly in diseases caused by micro-organisms or other parasites that drugs may be definitely curative. Older preparations of this type include, notably, antiseptics, anthelmintics, and " specific " remedies such as quinine for malaria, mercury for syphilis, and ipecacuanha for amoebic dysentery. Until very recent years such remedies were discovered, and could only be discovered, by clinical experiments on persons suffering from these diseases. The action of drugs upon *normal* animals could not provide a basis for the study of the effect of drugs in disease, if in that disease the drug acted, partly or wholly, upon an infective agent. It is true that some indication as to possible " specific " therapy might be obtained from comparative pharmacology. For example, the action of quinine on non-parasitic protozoa might suggest its use in a disease due to pathogenic protozoa.

But it was soon realized that it was of little, or even of misleading, value to determine the pharmacological or toxicological action of a drug on a pathogenic organism as a sole or separate problem. And this for two important reasons. In the first place it was found that the action of drugs on micro-organisms was often highly specific. A drug which would readily kill one micro-organism might have relatively little effect on a very nearly related micro-organism—for example, quinine was less effective in one type of malaria than in another. Consequently the final test of the value of a drug in a parasitic disease had to be carried out strictly on the particular organism causing the disease and on no other. Secondly, it was found that in the case of many, if not most, parasitic diseases in which it was believed that this cure was due to the toxic action of the drug on the causal organism this action was not immediate, simple, or direct, but was modified by the action of the drug on the host. The practical outcome of these discoveries was that the only possible way of determining with any certainty the curative value of a drug in a disease caused by a pathogenic organism was to test the drug in an animal affected with the disease. The action of the drug had to be determined on the complex of host + parasite. The value of quinine in malaria had been so discovered by experiments on men naturally infected with the malarial parasite.

The possibility of investigating the action of drugs on disease as a complex would, however, be for many reasons vastly simplified and extended if experiments could be done on laboratory animals infected with a particular disease ; and the nearer such a disease resembled a disease in man the more likely would success be attained in therapeutics. This, which might have been anticipated to be the easiest part of the problem, has often turned out to be the most difficult.

A great stimulus was given to chemotherapeutic research by Ehrlich's discovery of salvarsan, and one is often asked why advance in the treatment of trypanosome diseases has been so rapid as compared with most other diseases. There are two chief reasons. In the first place, trypanosome infections can be readily produced in small laboratory mammals—for example, mice—with a consequent reduction in the cost of experiment and in accommodation required. Secondly, the parasite is easily recog-

nized in the blood and the course of the infection followed; and the most easily observed end-point, death, is with some such infections a very constant time-point. It is relatively easy to decide if a drug has even a slight curative action on the disease. One reason, therefore, for the success of the attack that has been made on the problem of trypanosome diseases is simply the ease of experiment. In other diseases this condition has not been at first forthcoming. For example, human malaria cannot as yet be produced in laboratory mammals, but a type of malarial infection occurs in birds, on which chemotherapeutic research has been carried out which has already borne fruit in the treatment of malaria in man. Similarly, laboratory animals can now be infected with amoebic dysentery, and even, more recently, with leishmaniasis.

For chemotherapeutic research the production of the disease under suitable experimental conditions is, however, not the only necessity. One must also have the potential or reputed remedy. For this second necessity we have hitherto been largely dependent on observations on disease in man. The efficacy of cinchona in malaria and of ipecacuanha in dysentery has been known for centuries. An entirely new plan of attack has, however, been rendered possible by the advances of chemical science. Once the chemical and structural constitution of the alkaloids of cinchona and ipecacuanha were known, it became possible for the chemist to modify these alkaloids in various directions, or to synthesize alkaloids resembling them in certain particulars; and, if these new compounds were chemotherapeutically tested, there was the possibility that some of them might be superior, as therapeutic agents, to the original alkaloids.

Investigations so far have tended to show that the natural alkaloids are superior to artificial alkaloids, whether as therapeutic or as pharmacological agents; so much so, that many have adopted the view that no artificial alkaloid, especially if unrelated to the natural alkaloid, will prove equal to the natural alkaloids as therapeutic agents. While the evidence at present may support that view, I think it is nevertheless fallacious. It was natural that pharmacology and chemotherapy should at first concern themselves with substances which were already known to exert physiological or therapeutic action, and, therefore, in the earlier stages of this science, the great mass of the investigations have been occupied with natural alkaloids or derivatives of them.

What steps have we taken that this country should play a worthy, if not a leading, part in chemotherapeutic research? The answer is that we are doing little that is commensurate with the importance of the subject. It is, I think, beyond dispute that at the present time there is a great waste of opportunity. We have many laboratories actively engaged in making new chemical compounds either for immediately scientific or for commercial purposes. Only a trifling number of such compounds ever receive even a perfunctory pharmacological investigation.

Experimental Therapeutics and Suggestions for Advance

The value of experimental pharmacology and of chemotherapy rests ultimately, however, upon the application of the results so obtained to the treatment of naturally occurring disease in man and other animals. The final and crucial test is the test of the effect of a drug in disease in man. It may therefore be correctly surmised that human experimental therapeutics will require, so far as possible, the same amenities of experiment, the same forethought, skill, and co-operation as the ancillary sciences. The following are some considerations that I venture to put forward.

1. Medical students ought to be taught therapeutics just as thoroughly as they are now taught diagnosis or pathology. They should not only receive oral instruction in the knowledge of therapeutics, but should be taught practically the methods of therapeutic investigation. In connexion with this one might have reason to hope that the general practitioner, who has ample opportunities for observing the therapeutic effects of drugs, might play a more important part in the advance of therapeutics than he has done for the last hundred years. Many observant general practitioners find out, as the result of their experiences, points about the effects of drugs or their side actions which may seem too insignificant to warrant publication. Though these points taken singly may seem of little importance, taken in the aggregate the experiences of the general practitioner, if they could be collected and assessed, would certainly assist greatly in the advance of practical therapeutics.

2. Teaching implies teachers. While perhaps every clinical teacher deals more or less with the treatment of disease, few of them would regard therapeutics as their main business. The University of Edinburgh is, so far as I know, the only teaching medical school in this country which has a whole-time chair of therapeutics.

3. The problem of discarding useless remedies is still with us, because new remedies are thrust on the medical market by drug manufacturers in increasing numbers. Many drug manufacturers in various parts of the world are now actively engaged in investigating new compounds. These investigations are expensive, and the manufacturer rightly looks to recoup himself for the expense by the profits on a new drug, if he can put it successfully on the market. Until we know more about the relations between chemical constitution and physiological action, this type of research must remain largely as a gamble, so far as concerns the discovery of a successful remedy. The testing of a new drug on the therapeutic side has often been perfunctory and done by medical men who have neither the training nor the facilities for arriving at a correct estimate of therapeutic value. This difficulty has recently been at least partly removed by the institution of the Therapeutic Trials Committee of the Medical Research Council. A manufacturer can now submit a new drug for the consideration of this committee, and the committee can, if it believes that the pharmacological indications justify a therapeutic trial, make arrangements for a scientific and thorough investigation of the therapeutic merits of the drug. Of the success of this venture it is too early to speak, but if, as a result of the operations of this committee, drugs will not in future be put on the market without reasonable evidence to justify the claims made for them, the gain will be great.

4. In the provision of teaching and research in therapeutics it might be of advantage to have at least one large hospital in this country which should definitely concentrate its main energies upon therapeutic research and upon post-graduate instruction. It is of course impossible and unthinkable that therapeutics should be separated from the rest of medicine, and no one would suggest that this should be done; but research and teaching need not be on the same plan in all hospitals. At least one hospital might, so far as teaching and research go, take the diagnosis, aetiology, etc., as read, and concentrate its energies upon therapeutic investigation. It might attract the type of man who is interested in this class of work, and a few physicians with this training and interest would help to leaven the whole lump.

5. Some organization is wanted for sifting and promulgating the knowledge of therapeutics. One of the most serious problems that confronts the worker in all sciences at the present time—and perhaps especially medical science—is to keep pace with the accumulations

of knowledge. Medical research is increasing in different parts of the world, and new journals continue to appear. The difficulty of assessing the present state of knowledge is perhaps nowhere greater than in therapeutics, largely on account of the number of publications in which the information must be sought. For instance, there is scarcely any kind of medical publication in which it would not be possible to find some reference to quinine. If a person were to begin to make a complete study of the chemistry, pharmacology, toxicology, and therapeutics of quinine he might have to spend a good part of a lifetime in reading the literature on this single alkaloid. Anyone who begins now to research on such a subject is confronted with the heroic task of ascertaining what has already been done. With the rapid growth of medical research this task becomes more formidable from year to year. It is a realization of this difficulty that has prompted in recent years the creation of special journals devoted to "abstracts" and "reviews." The difficulty of coping with even abstracted literature is becoming increasingly great. These methods of dissemination of knowledge, though a present aid, will before long break down under pressure, and some better method will have to be devised.

I have often wondered whether some such plan as I am about to sketch might not be feasible, though the time may not yet be ripe for it. Every country which engages in medical research should establish a bureau of pharmacology and therapeutics to which would be sent separate reprints of every paper dealing with these subjects. At present, certain privileged libraries in this country receive a copy of every book published in this country. It would be a problem differing rather in degree than in kind to have a similar system internationalized. It would require arrangement with publishers, for it could not be left to authors. Each national bureau would receive roughly as much as it gave. The advantages would be: (1) that the future literature on the subject would be complete in one special library in each country; (2) that it is better to have one complete library on a subject than several incomplete ones; and (3) that it is far easier to extract the desired information from a library consisting of separated pamphlets on one subject than from an ordinary library of volumes of journals, even if the latter are complete. May one go further and prophesy that the time may come when we shall have an institute which will combine laboratories for pharmacology and chemotherapy, a hospital for therapeutic research, and a bureau for sifting and promulgating the advances in knowledge? We have an elaborate organization, with a Ministry, for the prevention of disease; we have no such organization as yet for the treatment of it.

SUMMARY

The past century has been in the main an era of aetiology and diagnosis; the coming century bids fair to be an era of therapeutics. For taking a worthy part in the advances that are certain to be made in the treatment of disease we are in this country none too well organized. We need more laboratories adequately equipped for research in pharmacology and chemotherapy, subjects which will play an increasingly important part in the advance of therapeutics proper. We need more researchers and more careers open to them.

Both in teaching and in investigation more attention must be paid to the assessment of the remedial value of drugs in man. Advance in the treatment of disease might be facilitated by having at least one hospital definitely devoted to research in therapeutics and by the creation of a specialized bureau and library for collecting and disseminating the knowledge of these subjects.

CHOLESTEROL METABOLISM IN DISEASE*

BY

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Cholesterol is an integral constituent of all cells and organs of the animal body. All body fluids contain some cholesterol; even urine contains traces, much augmented in the urine of patients suffering from nephrosis. It exists in the body in the free or alcoholic condition, and also in the form of its esters with the higher fatty acids. These two forms are not equally distributed.

The importance of cholesterol from the point of view of the pathologist was increased by the discovery that under certain physiological conditions—for example, pregnancy—the cholesterol content of the blood might be increased above normal; that in infective conditions at the height of fever the cholesterol of the blood was subnormal—hypocholesterolaemia; that in morbid conditions, such as in various forms of nephritis, cholelithiasis, diabetes, etc., the sterol content of the blood was increased often far above normal value—hypercholesterolaemia. The interest of pathologists was further stimulated by the discovery, I think in Professor Aschoff's laboratory, that the doubly refracting crystals or droplets found histologically in the normal suprarenal cortex, in atheromatous intima, in inflamed kidney, and in other organs, consisted of cholesterol esters; by the observations of Ransom that cholesterol has the property of inhibiting the haemolytic action of saponins; and by the work of the Russian observers, Anitschkow and Chalatow, showing that prolonged feeding to rabbits leads to cholesterol infiltration of the various tissues, the changes in which have been considered to resemble human pathological processes—for example, atherosclerosis.

Space forbids a detailed history of progress in this subject, but I should like, before going on to an account of some recent work, to acknowledge how much we owe to Chauffard and his co-workers in France, and more especially to Professor Aschoff and his school in Germany.

During the past twenty years progress on the chemical side has been more rapid than on the physiological side. Thanks largely to the brilliant work of A. Windaus and of H. Wieland on the oxidative breakdown of cholesterol, and of the bile acids, it has been possible to assign structural formulae, having a high degree of probability, to these substances, and to show that there is an intimate chemical relation between cholesterol and the bile acids.

Cholesterol is an unsaturated secondary alcohol of the molecular formula $C_{27}H_{46}O$, derived from the parent saturated hydrocarbon cholestane $C_{27}H_{48}$. By catalytic reduction the double link is saturated with the formation of bihydrocholesterol or β cholestanol, a saturated secondary alcohol. Coprosterol, which occurs in human faeces, is a stereo-isomer of β cholestanol, the difference depending on a steric rearrangement of the substituent groups at one of the carbon atoms. The parent hydrocarbon, coprostane, is a stereo-isomer of cholestane.

Various artificial isomers of cholesterol have been prepared in the laboratory, the most interesting being the very labile "allocholesterol," which very readily changes into ordinary cholesterol, particularly in acid media. This allocholesterol is readily reduced *in vitro* to coprosterol.

The specific bile acids and cholesterol possess the same carbon structure, except that in the bile acids an isopropyl group $(CH_3)_2CH$ has been eliminated from the side chain.

The bile acids which have been most studied are those of ox bile—namely, lithocholic acid (3 oxycholanic acid) deoxycholic acid (3.7 dioxycholanic acid) and cholic acid

* Read in opening a discussion in the Section of Pathology at the Centenary Meeting of the British Medical Association, London, 1932.

(3.7.12 trioxycholanic acid), which are derivatives of a parent acid, cholanic acid ($C_{24}H_{40}O_2$). In goose, ox, and human bile another deoxycholic acid, with the hydroxyl group in position 3 and 12, is also found—namely, chenor anthropo-deoxycholic acid. These acids, though they do occur as such in the bile, are usually coupled with glycine or with taurine. They belong to the same stereoisomeric series as coprosterol. However, from pig's bile a hyodeoxycholic acid (3 : 13 deoxycholanic acid) has been isolated which belongs to the same stereo-chemical series as cholesterol. The following scheme shows these relations:

(Parent hydrocarbon)	Cholestane		Coprostane
	↓		↓
(Unsaturated alcohol)	Cholesterol	⇄	Allocholesterol
	↓		↓
(Saturated alcohol)	β Cholestanol		Coprosterol
	↓		↓
(Bile acid)	Hyodeoxycholic acid		Cholanic acid and hydroxy derivatives

The above-mentioned constitutional formulae, though probably correct in the main, must still be regarded as tentative, as they are based on a study of analytical reactions. The formulae have yet to be confirmed by synthetic methods.

It is important to note that in vertebrate animals the only unsaturated sterol isolated from tissue substance is common cholesterol. Schönheimer has, however, recently found that this cholesterol is generally accompanied by small quantities of β cholestanol, varying in different tissues from 1 to 5 per cent. of the total sterol. In contrast to the sterols, many different bile acids, with considerably divergent properties, have been isolated from the bile of different species of animals. Furthermore, in the different animals the acids, even though the same, are present in very different proportions. Consequently in this domain the results of animal experiment are not necessarily applicable in human physiology.

At the present time we have little or no precise information as to the functions of cholesterol in the economy of the cells or of the whole organism, nor have we the data on which to base a sound comprehensive theory of the sterol metabolism (in the wide sense) or even effectively to criticize hypotheses propounded from time to time.

In the study of sterol metabolism in the human subject attention has been mainly directed to the blood and excreta. Other organs can, as a rule, be dealt with only post mortem. In this paper I propose to draw your attention briefly to some phenomena in pregnancy and to some diseases marked by disturbance of the sterol metabolism. I have selected mainly those on which I have had opportunity of working.

Before dealing with these subjects I must mention certain biochemical facts, as to the origin and fate of the cholesterol in the body, which I think must be taken into account in any interpretation of the results obtained in disease.

Many years ago, from the examination of very large quantities of the excreta of herbivorous animals "at grass"—horse, cow, sheep, rabbit—I found that the material contained no recognizable trace of cholesterol. The main crystalline product isolated was a paraffin alcohol contained in grass, and feeding experiments showed that it passed through the intestine of the rabbit unchanged. (We altered the name of this substance to chortosterol under the impression that it was a saturated sterol, since it had the composition $C_{27}H_{54}O$ or $C_{27}H_{56}O$. I now know that it was really an open chain saturated paraffin alcohol.) Small quantities of phytosterol were also isolated, and, later on, a few milligrams of a similar substance, which from my notes I now recognize was β cholestanol.

Now the bile of these animals contains quite readily estimable amounts of cholesterol, 0.02 to 0.07 per cent., so that had this cholesterol, poured into the intestine with the bile, been excreted, we could scarcely have failed to isolate some. Dorée and I were therefore led, from this and other facts then available, to formulate the following working hypothesis:

1. Cholesterol is a constant constituent of all cells, and when these cells are broken down in the life process the cholesterol is not excreted as a waste product, but is utilized in the formation of new cells.
2. A function of the liver is to break down dead cells—for example, blood corpuscles—and eliminate their cholesterol in the bile.
3. After the bile has been poured into the intestines in the process of digestion the cholesterol is reabsorbed, probably in the form of esters, along with the bile salts, and carried by the blood to the various centres and tissues for reincorporation into the constitution of new cells.

I believe the destruction of red corpuscles is now attributed to the reticulo-endothelial system in general.

This hypothesis received considerable support from feeding experiments, and from the careful investigations of Mueller (1915), who showed by analyses of chyle, obtained from thoracic duct fistulae in dogs, that cholesterol is readily absorbed from the intestinal tract through the chyle, and may be recognized and measured in the contents of the thoracic duct. This work of Mueller has been amply confirmed and extended, most recently by Schönheimer. Since then I have found no reason to doubt the reality of this cholesterol cycle, though I admit, and shall show presently, that it is by no means the whole story.

Some explanation of the mechanism of the cycle is afforded by the work of Wieland and Sorge (1916), who found that deoxycholic acid formed stable molecular compounds with the higher fatty acids—for example, $8C_{24}H_{40}O_4$ and $C_{18}H_{36}O_2$ with stearic acid. The choleic acids isolated from bile were a mixture of such stearic, palmitic, and oleic acid compounds. These compounds are very stable, crystallize well, and their salts are easily soluble in water. Besides the fatty acids, many other substances form somewhat similar compounds. Materials which are insoluble in water, such as naphthalene, xylene, alkaloids, cholesterol, camphor, etc., are brought into solution by an aqueous solution of deoxycholate. This power of uniting with insoluble substances to form soluble products Wieland called the "choleic acid principle," and concluded that it had an important function in transporting insoluble substances, such as fat and fatty acids and cholesterol, through the intestinal wall.

It has recently been shown by Schönheimer that sterols of the vegetable kingdom are not absorbed by the animal organism from food, or when administered as such, and, indeed, in tissues behave as foreign bodies ; consequently any waste of cholesterol in these herbivora must be made up by synthesis. That cholesterol is synthesized in the body clearly follows from balance experiments by Gardner and Fox, Thannhauser and others, and the more direct experiments of Beumer, Channon, Randles and Knudsen, and others. We have no real evidence as to the seat of such synthesis, though various hypotheses have been advanced and have led to much discussion.

In carnivora and omnivora an excretory mechanism appears to exist, so that there is always a quantity of sterol excreted in the faeces: this is mainly in the form of cholesterol or coprosterol, or both. In man this excretion has been shown by balance experiments to be always greater in quantity than the amount ingested with the food. Fox and I, making use of very reliable material obtained by a subcommittee of the Royal Society Food (War) Committee, in experiments on the digestibility of bread, investigated the sterol balance. In the experiments the diets were consumed for periods of ten days, the six significant days being the fourth to the ninth inclusive. The daily intake and output of sterols precipitable by digitonin have been estimated, and, taking an average of all subjects, there is a negative balance of 0.31 gram per day. It has long been known that the sterol of adult faeces consists largely of coprosterol, accompanied by smaller quantities of β cholestanol and sometimes cholesterol. Since Voit's classical experiment on the production of a faeces-like material, containing fat, in an isolated loop of small intestine, evidence has gradually accumulated that sterols may be excreted in the intestinal lumen otherwise than with the bile.

In 1911 Böhm, in a paper the importance of which was perhaps not realized at the time, reported on the contents of a completely closed loop, of some fourteen years' standing, in the intestine of a human subject. The contents were sterile, and the sterol present was found to consist of β cholestanol ; this could only have got there by excretion through the walls of the loop.

Recently Schönheimer and von Behring, working on dogs, examined the excretion of a large intestine which had been isolated by the performance of a complete ileostomy. The sterol isolated was β cholestanol, but no coprosterol could be detected. The appearance of the material was similar to that described by Böhm, and an examination of the mucous membrane of the large intestine after killing the animal showed no histological changes. Clearly there is another way of excretion of sterols in the faeces besides that of the bile. Schönheimer and his co-workers have also shown by thoracic duct experiments that neither β cholestanol nor coprosterol is absorbed through the chyle.

It is generally believed that coprosterol is produced by the reduction of cholesterol in the intestine by bacterial action. The evidence for this is not positively strong, as nobody has succeeded in producing this change *in vitro* by the action of organisms. It is significant, however, that in the faeces of infants in the milk stage no coprosterol is formed. The sterol I have found to consist almost entirely of pure cholesterol, though traces of β cholestanol, such as have been found by Schönheimer in the cholesterol of most organs, are not excluded. Indeed he has detected this in the intestinal contents of a foetus.

Fox and I made a number of balance experiments on breast-fed infants. During the first week of life there was a negative balance of 0.14 gram per day. During the second and third weeks the average balance was 0.002. Out of the seven cases five showed a virtual balance, any difference being within the errors of experiment. One case showed a marked positive balance. In the case of children between 7 weeks and 10 months an average positive balance—that is, excess of intake over output—of +0.069 gram per day was obtained. Six of the seven cases showed a positive balance. At what stage of life, or alimentation, the process of reduction to coprosterol begins we do not know. Clearly, in the light of recent work the production of coprosterol and bihydrocholesterol in the intestines would limit the absorption of cholesterol.

There appears to be some difference in degree, if not in type, between herbivora and carnivora and omnivora with regard to the effects of absorption of cholesterol. It has been long known from the work of Ignatowski, Starokadomski, Stukey, and Chalatow that feeding rabbits with various animal foods, above all yolk of eggs, produces intimal changes in the aorta and accumulation of anisotropic fats in the liver and other organs. This led Chalatow and Anitschkow to try the effect of administering cholesterol dissolved in sunflower oil: they produced thereby accumulation of lipoids, chiefly doubly refracting esters in the suprarenal cortex, in the liver, spleen, and lymph glands, and later a deposit in the intima of the aorta, together with hyperplasia of the elastica—similar changes to those of atherosclerosis in man. This work was criticized by Wacher and Hueck because of the use of a stomach tube and the feeding of unaccustomed food. They fed rabbits by the mouth with oats mixed with cholesterol, and found an increase in the blood compared with normal of both free and ester cholesterol, as well as an accumulation of doubly refracting fats in the suprarenals, liver, and other places, and also aortic changes of the kind mentioned. They were unable to produce aortic changes in either dogs or cats, though feeding was prolonged for two months. Anitschkow also failed to find arterial change in rats fed with cholesterol for five months. Yuasa, by very prolonged feeding with diets containing added cholesterol, produced the so-called cholesterol disease in mice, rats, and cats, but only in half of the rats and mice was atherosclerosis observed, and in none of the cats. He thinks that his results do not point to any essential difference in principle between the metabolism of herbivora and carnivora, but that there is a difference in the sensitiveness of the intima of the arteries of different kinds of animals towards excess of cholesterol.

In all these observations it is tacitly assumed that cholesterol deposition in the arterial intima is identical with the process of the laying down of cholesterol in the liver, suprarenal, and other organs. From my own work on the feeding of rabbits and cats with cholesterol, in as physiological a manner as possible, for periods of about ten to twelve days, the variation produced in the cholesterol ester content of the liver, at any rate, is hardly pathological; within fairly wide limits it is clearly a physiological process. On the other hand, the deposition of cholesterol in the arteries, when it occurs, can scarcely be considered to be physiological. In man there is no evidence whatever to associate the occurrence of atherosclerosis with the exogenous cholesterol metabolism.

As a result of Windaus's chemical work, it was suggested that the bile acids are derived in the organism from cholesterol. Unfortunately the methods available for the estimation of bile acids are only rough, and we have no means of making any quantitative estimation of the relative proportions of the different bile acids. Thannhauser and his co-workers, by injection of colloidal cholesterol solutions into the blood stream, found, using bile-fistula dogs, little or no change in the cholic acid content of the bile excreted over a definite period ; but on injecting allocholesterol in a similar manner they obtained an increased output of bile acid. This result is interesting, and perhaps significant, but can scarcely be accepted as proving the conversion of allocholesterol into cholic acid, for even if we assume that the bile acid estimations are correct, the weight of bile acid formed was much greater in weight than the weight of the allocholesterol injected. However, nobody has yet succeeded in bringing forward any evidence of the existence of allocholesterol or coprosterol in tissues.

Alimentary Hypercholesterolaemia

The data given in the literature are very conflicting. Experiments made by myself and Gainsborough have shown that the level of the cholesterol content of the plasma, taken before breakfast, can be raised or lowered by sufficiently prolonged feeding with diets of high or low cholesterol content. Such changes are most marked as regards the cholesterol in ester form ; the free cholesterol remains practically constant. We found that as a result of a single meal alimentary hypercholesterolaemia (in the ordinarily accepted sense) does not occur, and there is no obvious connexion between the amount of cholesterol ingested and the cholesterol level of the plasma during digestion. During the digestive process changes in the cholesterol content of the plasma frequently occur, sometimes as an increase, sometimes as a decrease, compared with fasting values. Often a marked temporary disturbance of the ester to total ratio is observed. These peculiar changes cannot be explained by the influx of the cholesterol absorbed from the alimentary canal, but must be considered as evidence of an active endogenous metabolism in which cholesterol takes part during digestion.

The cholesterol content of the " fasting " plasma varies markedly in different healthy individuals, but is fairly constant for the individual himself, even over long periods. The following table summarizes the results of our own observations on some fifty healthy individuals of both sexes ; the figures represent grams per 100 grams of plasma.

	Total Cholesterol		Free Cholesterol		Ester Cholesterol	
	Average	Limits of Variation	Average	Limits of Variation	Average	Limits of Variation
Male ...	0.170	0.11-0.22	0.050	0.005-0.082	0.120	0.080-0.14
Female...	0.153	0.08-0.23	0.054	0.020-0.094	0.100	0.054-0.14

These values would, of course, include any traces of β cholestanol if present. The ester cholesterol usually forms from 60 to 70 per cent. of the total cholesterol. The cholesterol and cholesterol esters in the plasma are not simply present in colloidal solution, or suspension, as such, but, as Gainsborough and I have shown, are in intimate physical or perhaps loose chemical union with the proteins, particularly the globulins.

CHOLESTEROL METABOLISM DURING PREGNANCY

Blood analyses during pregnancy were first reported by Chauffard. Since then numerous papers have been published, but perhaps the most extensive data have been given by Tyler and Underhill (1925). The general conclusion drawn is that hypercholesterolaemia occurs in pregnancy and the early puerperium. Tyler and Underhill used whole blood, and estimated both free and ester cholesterol values. The use of whole blood tends to mask certain changes, since the cholesterol of the red cells is mainly, if not entirely, in the free state, and is fairly constant in percentage, whereas the cholesterol of the plasma is present in both free and ester forms, the latter usually in preponderating quantity. Hence an analysis of whole blood, including the almost constant sterol content of the red cell, tends to hide the value of quite large changes in the plasma cholesterol. Another disturbing factor is the anaemia of pregnancy, which varies markedly in different individuals and is often of considerable degree. In our own experiments we analysed the plasma. Blood specimens were taken at monthly intervals before parturition and once or twice during the period of confinement. We found: (1) that the free cholesterol of the plasma increases during pregnancy up to a maximum at about the thirtieth week; concurrently the ester cholesterol falls to a minimum at about the same time; (2) from the thirtieth week, more or less approximately, the amount of free cholesterol decreases, and the ester increases till an almost normal ratio of free to ester cholesterol is attained before or near parturition; (3) the plasma cholesterol values are generally normal in the first week or two of the puerperium; (4) some cases show a definite total hypercholesterolaemia in which the total cholesterol figures run roughly parallel to the free cholesterol values, a result in general agreement with those of earlier observers, and our actual figures are of much the same order as theirs.

As we know nothing whatever of the function of cholesterol in the cell, and very little of the part it plays in the general metabolism, I will not indulge in hypothetical explanations, but simply give the results of our observations. In order to explain the fact, if it be a fact, that 75 per cent. of cases of cholelithiasis occur in women, some writers have suggested that hypercholesterolaemia occurring in repeated pregnancies is of paramount importance in the formation of gall-stones. This suggestion, however, scarcely helps to explain the occurrence in men; also an examination of post-mortem records at St. George's Hospital showed that cholelithiasis had not occurred in cases of subacute parenchymatous nephritis, where hypercholesterolaemia rules much higher than in pregnancy.

BLOOD CHOLESTEROL IN BILIARY AND HEPATIC DISEASE

It is obvious from what I have said that the percentage of cholesterol in plasma is the resultant of many factors, the balance of which determines the plasma cholesterol level at the moment the blood is taken.

Gainsborough and I thought it possible that evidence as regards endogenous metabolism might be obtained by studying the variation of plasma cholesterol in disease of the liver and bile passages. It soon became evident to us that the metabolism was disturbed grossly and in a complex manner in such conditions, but that the one common factor which could be correlated with these changes was the occurrence of jaundice.

The earlier French workers generally believed hypercholesterolaemia to be a constant feature of cholelithiasis, and a causal factor of the disease. Their observations were added to by many workers, until Campbell showed that hypercholesterolaemia only occurred when the disease was accompanied by jaundice. Such increase of blood cholesterol has been explained as a simple retention phenomenon, due to the failure of the excretion of the cholesterol of the bile.

Recently Thannhauser and Schaber found a disturbance of the percentage of the total cholesterol as ester, and noted a sudden fall of the ester values almost to the vanishing point, which they refer to as "estersturz." This they regard as due to a failure of the esterifying power of the liver cells, the result of parenchymatous damage.

Bürger and Habs, Stern and Suchantke, and Adler and Lemel criticized these authors, and were unable to confirm the occurrence of "estersturz." They agree, however, with Thannhauser and Schaber's finding of hypercholesterolaemia in biliary stasis, with simultaneous occurrence of comparatively low ester values. They regard the hypercholesterolaemia as due to the retention in the blood of the free cholesterol normally excreted with the bile, and believe that this suffices to account for the lowering of the ester to total ratio.

In our work we examined some thirty-five cases. In order to eliminate the disturbing factor of digestion the blood was taken while the patient was in the "fasting" condition—that is, before breakfast. It is rather important to stress the fact that jaundice from biliary obstruction and the actual biliary obstruction are not necessarily contemporaneous, and that the only plain clinical evidence of existing biliary obstruction is the absence of bile pigment from the faeces. For example, of two of our cases, both extremely jaundiced from the impaction of a gall-stone in the common bile duct, the one had had persistent colourless faeces for eighteen months, while the other, though even more deeply jaundiced, had occasionally, during ten months, periods of coloured stools, so that the obstruction must have been intermittent. The former showed marked hypercholesterolaemia while the latter did not, so that even though in this latter case most of the bile was probably retained, the cholesterol picture had not been so disturbed as the former. The analyses were:

Cholesterol per 100 grams of Plasma

	Free	Ester	Total	Percentage of Total Cholesterol as Ester
(1) Massive jaundice during 18 months. Stools clay-coloured	0.3584	0.2391	0.5975	40.6
(2) Massive jaundice for 10 months, but obstruction intermittent, with faeces occasionally coloured	0.0920	0.0671	0.1600	41.9

In seventeen cases of uncomplicated cholelithiasis without jaundice there was no hypercholesterolaemia and the percentage of the total as esters was within normal limits.

An examination of the data of the other eighteen cases, in which failure of bile to flow into the intestine had been known to occur, and in which, with two exceptions, jaundice had been present, reveals two different types of changes in the blood cholesterol picture.

(*a*) On establishment of biliary obstruction there soon appears a lowering of the cholesterol ester content of the plasma, almost to the vanishing point. In some cases, and at the same time, the free cholesterol may be normal or slightly increased. If the biliary obstruction is relieved the picture returns quickly to normal.

(*b*) If absolute biliary obstruction persists a true hypercholesterolaemia ensues, with a low ester total ratio of 30 to 50 per cent.

Blood picture (*a*) was well illustrated in eight of our cases. I give one example. This case, of cholelithiasis, during a period of transient jaundice was treated with deoxycholic acid and dehydrocholic acid, with the result that in three days, with the establishment of the bile flow into the intestine, the cholesterol ester content of the plasma returned to normal.

Sex	Presence of Jaundice	Date	Cholesterol per 100 grams of Plasma			Per cent. of Total as Ester	Remarks
			Free	Ester	Total		
M.	+	29/12/27	0.0674	0.0048	0.0727	6.65	Gall stones visible clearly by *x* rays
	+	3/1/28	0.0846	0.0023	0.0869	2.65	Deoxycholic acid from 29/12/27 to 3/1/28. Faeces pale
	0	6/1/28	0.0817	0.1331	0.2148	62.6	Dehydrocholic acid intravenously 3/1/28 to 6/1/28. Faeces normal in colour
	0	6/2/28	0.0901	0.1728	0.2626	65	—

True hypercholesterolaemia of high degree, involving both forms of cholesterol, was well shown in three cases where the biliary obstruction had been complete for a considerable time. The figures in the case quoted above may serve in illustration.

A hint as to the significance of the first type of change was obtained from study of two cases with post-operative biliary fistulae. In one of these the fistula was apparently complete for six months, and the blood picture showed a remarkable "estersturz," the ester cholesterol falling to 0.009 per cent. Now the only common factor between these cases and those of jaundice showing the same blood picture is the absence of bile from the intestine. We see that by whatever means the bile is deviated from the intestine, whether by obstruction with biliary stasis or by obstruction without stasis (the bile flowing away freely and completely through an external fistula), the phenomenon of ester-vanishing tends to occur. Such absence of bile from the intestine leads, as we know, to a failure of fat and sterol absorption, which must be significant, and must be correlated closely with the diminution of cholesterol ester in the plasma. The re-establishment of normal bile flow and of fat absorption lead, in the case quoted, to an amazingly rapid return of cholesterol ester to the plasma to the extent of 4.3 grams in three days.

Consideration of the later-occurring hypercholesterolaemia presents certain difficulties, for, in spite of persistent failure of fat absorption, cholesterol in both forms piles up in the plasma, and though the ester form lags behind the free, its value can still reach a high figure. If the hypercholesterolaemia is due solely to the retention of the free cholesterol of the bile it might be suggested that some of the retained cholesterol is esterified by mobilization of fat from the fat depots. This utilization of the body stores of fat probably also liberates the associated cholesterol in these stores, and this possibility has been suggested as an explanation of the hypercholesterolaemia which occurs in starving animals. However, the hypercholesterolaemia which occurs in biliary obstruction is generally believed to be due to cholesterol retention ; but when we consider that in bile stasis there is probably at the same time a failure of alimentary cholesterol absorption, it is by no means obvious that cholesterol retention is not balanced by this failure. It might be possible to obtain further evidence on this problem by performing balance experiments on patients with jaundice, or with complete biliary fistula, by feeding on a sterol-free diet. Such experiments would be rendered very difficult, however, by the constipation shown by these patients.

NEPHRITIS

Hypercholesterolaemia is present in all those cases which possess the "nephrotic" syndrome, marked by diffuse parenchymatous degeneration, heavy albuminuria, changes in the plasma proteins, and with oedema as the chief symptom. Consequently, increases of plasma cholesterol are found in those cases of subacute and chronic nephritis of prolonged duration, where albuminuria is predominant and haematuria insignificant, and which range, as Gainsborough has stated, from cases of glomerulo-nephritis in which the initial nephrotic state is more or less rapidly followed by sclerosis and contraction of the kidneys, by gradual transition to those cases of so-called "pure nephrosis," where renal sclerosis and its accompanying symptoms are not observed. The total cholesterol in the plasma may reach as much as 1 per cent., and the percentage of total in form of ester may assume abnormal value in either direction. This high level of cholesterol is present throughout the course of these cases of nephritis so long as there is any tendency to oedema, and it persists in cases of subacute parenchymatous nephritis for long periods, even though oedema is temporarily absent. After a more or less prolonged period the tendency to oedema is replaced by tendency to vascular changes, increase of blood pressure, and signs of nitrogen retention, and about the same time the hypercholesterolaemia diminishes.

The cause of this hypercholesterolaemia is not known, but may perhaps be related to the disturbance of the plasma proteins resulting from proteinuria. Gainsborough and I estimated the cholesterol of the carefully filtered urine of several patients showing hypercholesterolaemia, and found from 16 to 41 mg. per day were excreted, the excretion in the urine by normal persons being at most 1.7 to 4 mg. per day. As in the case of plasma, we found the same attraction between the sterols and the proteins of the urine, and the attraction is most marked as regards the globulin.

Hypercholesterolaemia is not found in cases of interstitial nephritis, in arteriosclerotic kidney, or in arteriosclerosis.

Many observers have reported on the chemical analyses of kidney tissue in nephritis. Windaus gives the normal amount of cholesterol in fresh kidney as: free cholesterol 0.22 per cent., ester cholesterol 0.01 to 0.03 ; but in large white kidney: free 0.22 to 0.33 per cent., and ester cholesterol 0.09 to 0.65 per cent. Fex obtained similar results, showing that in cases of glomerular nephritis and of nephrosis the free cholesterol is hardly if at all increased, but the ester is greatly increased. He also found the liver and suprarenals in these cases were normal.

In a case of advanced chronic glomerulo-nephritis we found that, though the blood cholesterol was normal, the kidney was abnormally rich in ester: free 0.27 per cent., ester 0.2 per cent. In another case in which high hypercholesterolaemia had been noted a few months before death the kidney contained free 0.39 per cent. and ester 0.36 per cent. The analysis of other organs—liver, lung, spleen—was approximately within normal limits.

MYXOEDEMA

The total cholesterol of plasma in this condition may be increased by nearly 50 per cent. above normal. Epstein and Lander thought that blood cholesterol was inversely proportional to the basal metabolic rate, and they suggested an analogy between myxoedema and pure "nephrosis," where the basal metabolic ratio is also below normal. This argument was then used to explain the occasional beneficial results of thyroid medication in "nephrosis." However, Gainsborough and I found that this relation of basal metabolic rate and blood cholesterol does not exist in states of hyperthyroidism where, as in exophthalmic goitre, the blood cholesterol is within normal limits.

It may be thought that I have laid too much stress on the chemical aspects of the problems of sterol metabolism. Another method of approach, however, to these problems—in some aspects just as important—is afforded by the histological study of pathological conditions in which deposits of cholesterol esters occur in the tissues, as in chronic nephritis, Niemann's disease, atherosclerosis and in xanthoma. In some of these the deposition of sterol is apparently not determined so much by a hypercholesterolaemia as by the local lesion, whatever may be its nature, as in atherosclerosis. In other cases the deposits seem definitely due to an increase in blood sterol. The contrast is well seen in cases of xanthoma. In xanthoma simplex the lesion is unassociated with hypercholesterolaemia. On the other hand, the hypercholesterolaemia in prolonged jaundice may lead to a widespread distribution of xanthomatous lesions, and that in diabetes may lead to a differently distributed but characteristic xanthoma eruption, whereas the high blood cholesterol of so-called nephrosis never, so far as I am aware, leads to such phenomena.

ATTENUATION AND PREVENTION OF MEASLES *

BY

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The subject which has been chosen for discussion to-day is ripe for consideration on practical lines. On the one hand we have a disease responsible for a large loss of life and much permanent disability among that section of the population that has been the subject of special solicitude from public health authorities. On the other hand research promises that if certain difficulties can be overcome the ravages of measles might be greatly curtailed.

We have been in possession of the requisite knowledge for several years, yet very little effort has been made—in this country at least—to apply it. The difficulties of applying it are real and formidable, but it is high time that an influential body of hygienists, such as that represented by the present meeting, should get together and decide what ought to be done. Fortunately the speakers who will follow me will be able to report that a start has already been made, and they will be able to inform you of schemes of measles prophylaxis which are in actual operation. In these circumstances I think I can best serve the purposes of the discussion by referring to some of the more general problems, leaving it to others to describe in detail their own work and the successes and difficulties with which they have met.

Aetiology of Measles

The first step in the prophylaxis of an infectious disease should be some knowledge of its aetiology, and of the aetiology of measles we know next to nothing. It is invidious, but necessary, to discount the great majority of observations which have been made on this subject. There have been recurrent claims that measles is due to a visible bacterium. The most recent of these have been by Caronia, who has isolated a small Gram-negative coccus; by Tunnicliff, who implicates a green-producing streptococcus; and by Ferry and Fisher, who state they have isolated a similar streptococcus which, they assert, produces a potent toxin. All three claims have been challenged by a majority of workers who have attempted to substantiate them, and I think it is quite fair to state that they have carried no conviction to bacteriologists in general.

In the absence of any clear evidence that measles is a bacterial disease it is customary to consider it as due to an ultra-microscopic virus. For this view there is a considerable amount of support, both direct and indirect. The high infectiousness of measles without any concomitant bacteriological findings, the long "silent" period of incubation, the nature of its exanthem, its rapid evolution and devolution, its great constancy of clinical aspect, and the consistent and lasting immunity conferred by an attack—all these point to a relation with a "virus" rather than with a bacterial disease.

The direct evidence that measles is due to a filterable virus, though perhaps not so solid as the importance of the subject demands, is none the less weighty. In the first place, the only experimental animal which has been shown at all convincingly to be susceptible to the disease is the monkey. Hektoen and Degkwitz have amply confirmed the results of earlier and less controlled experiments, going back to the time of Francis Home, that the blood of cases of measles in the early stage of this rash is infectious to children. But even here natural infection seems to be much more certain than any artificial method. Regarding the susceptibility of monkeys results have been conflicting, and though Blake and Trask have brought forward very convincing evidence of the susceptibility of *Macacus rhesus* I imagine that few bacteriologists would look upon their demonstration as a closed chapter. Perhaps the most important point in their work is that they appear to have demonstrated that Berkefeld N filtrates of nasopharyngeal washings could produce the disease in monkeys. In monkeys Blake and Trask observed, after an incubation period of six to ten days, conjunctivitis and a macular eruption, accompanied by a leucopenia, and followed by an immunity to further inoculation. It is to be regretted that at the time of Blake and Trask's experiments knowledge of the serum prophylaxis of measles was not enough advanced to suggest to them the counter-check of attempting to prevent their disease in monkeys by previous inoculation with serum. This, had it come off, would have added considerable support to their observations.

Possibilities of Immune Serum

As no domestic animal appears to be susceptible to the disease the only source of immune serum against measles available is the human being who has passed through the disease.

It is to Nicolle and Conseil (1918) that we owe the first experiments suggesting the utility of this serum. Since then many other workers, particularly Debré in France and Degkwitz in Germany, have worked out the details of the method of prophylaxis, the latter initiating the inquiry as to the value of serum taken from adults who have had measles in infancy. As to the value of serum taken in early convalescence, there is a very general agreement among workers throughout the world, many of whom have claimed 80 to 90 per cent. of successes if the serum is properly administered. But it would be unfair to suppress the fact that breakdowns are often met with, due sometimes to factors that are readily explicable but not infrequently occurring when no such explanations are forthcoming.

It is of course very difficult to collect conclusive facts on such a method of prophylaxis as this, and highly infectious as measles is, everyone meets with extraordinary vagaries in its infectiousness. Certainly individual successes in prophylaxis prove nothing. One must remember that remarkable results have been recorded using antibacterial serum and even normal horse serum. It is the cumulative experience derived from many efforts carried out all over the world that persuades us that convalescent serum is a really effective prophylactic reagent.

Practical Aspects

The use of convalescent serum is a procedure of very limited application, and whether the serum prophylaxis of measles is to be established as a practical public health measure will depend very much on the efficiency of serum taken from subjects who have once had measles. This I will call "adult," in contradistinction to "convalescent," serum. The published evidence in favour of its use has not up to now been convincing in all instances, though perhaps to-day we shall hear of valuable additions to this evidence.

Theory as well as experience, so far as it goes, suggests that serum is best collected immediately after the period of defervescence, for at this time such circulating antibody as is present is probably at a maximum. It is not to be supposed that this maximum is maintained

* Read in opening a discussion in the Section of Public Health at the Centenary Meeting of the British Medical Association, London, 1932.

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	+	3/1/28	0.0846	0.0023	0.0869	2.65	Deoxycholic acid from 29/12/27 to 3/1/28. Faeces pale
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True hypercholesterolaemia of high degree, involving both forms of cholesterol, was well shown in three cases where the biliary obstruction had been complete for a considerable time. The figures in the case quoted above may serve in illustration.

A hint as to the significance of the first type of change was obtained from study of two cases with post-operative biliary fistulae. In one of these the fistula was apparently complete for six months, and the blood picture showed a remarkable "estersturz," the ester cholesterol falling to 0.009 per cent. Now the only common factor between these cases and those of jaundice showing the same blood picture is the absence of bile from the intestine. We see that by whatever means the bile is deviated from the intestine, whether by obstruction with biliary stasis or by obstruction without stasis (the bile flowing away freely and completely through an external fistula), the phenomenon of ester-vanishing tends to occur. Such absence of bile from the intestine leads, as we know, to a failure of fat and sterol absorption, which must be significant, and must be correlated closely with the diminution of cholesterol ester in the plasma. The re-establishment of normal bile flow and of fat absorption lead, in the case quoted, to an amazingly rapid return of cholesterol ester to the plasma to the extent of 4.3 grams in three days.

Consideration of the later-occurring hypercholesterolaemia presents certain difficulties, for, in spite of persistent failure of fat absorption, cholesterol in both forms piles up in the plasma, and though the ester form lags behind the free, its value can still reach a high figure. If the hypercholesterolaemia is due solely to the retention of the free cholesterol of the bile it might be suggested that some of the retained cholesterol is esterified by mobilization of fat from the fat depots. This utilization of the body stores of fat probably also liberates the associated cholesterol in these stores, and this possibility has been suggested as an explanation of the hypercholesterolaemia which occurs in starving animals. However, the hypercholesterolaemia which occurs in biliary obstruction is generally believed to be due to cholesterol retention; but when we consider that in bile stasis there is probably at the same time a failure of alimentary cholesterol absorption, it is by no means obvious that cholesterol retention is not balanced by this failure. It might be possible to obtain further evidence on this problem by performing balance experiments on patients with jaundice, or with complete biliary fistula, by feeding on a sterol-free diet. Such experiments would be rendered very difficult, however, by the constipation shown by these patients.

NEPHRITIS

Hypercholesterolaemia is present in all those cases which possess the "nephrotic" syndrome, marked by diffuse parenchymatous degeneration, heavy albuminuria, changes in the plasma proteins, and with oedema as the chief symptom. Consequently, increases of plasma cholesterol are found in those cases of subacute and chronic nephritis of prolonged duration, where albuminuria is predominant and haematuria insignificant, and which range, as Gainsborough has stated, from cases of glomerulo-nephritis in which the initial nephrotic state is more or less rapidly followed by sclerosis and contraction of the kidneys, by gradual transition to those cases of so-called "pure nephrosis," where renal sclerosis and its accompanying symptoms are not observed. The total cholesterol in the plasma may reach as much as 1 per cent., and the percentage of total in form of ester may assume abnormal value in either direction. This high level of cholesterol is present throughout the course of these cases of nephritis so long as there is any tendency to oedema, and it persists in cases of subacute parenchymatous nephritis for long periods, even though oedema is temporarily absent. After a more or less prolonged period the tendency to oedema is replaced by tendency to vascular changes, increase of blood pressure, and signs of nitrogen retention, and about the same time the hypercholesterolaemia diminishes.

The cause of this hypercholesterolaemia is not known, but may perhaps be related to the disturbance of the plasma proteins resulting from proteinuria. Gainsborough and I estimated the cholesterol of the carefully filtered urine of several patients showing hypercholesterolaemia, and found from 16 to 41 mg. per day were excreted, the excretion in the urine by normal persons being at most 1.7 to 4 mg. per day. As in the case of plasma, we found the same attraction between the sterols and the proteins of the urine, and the attraction is most marked as regards the globulin.

Hypercholesterolaemia is not found in cases of interstitial nephritis, in arteriosclerotic kidney, or in arteriosclerosis.

Many observers have reported on the chemical analyses of kidney tissue in nephritis. Windaus gives the normal amount of cholesterol in fresh kidney as: free cholesterol 0.22 per cent., ester cholesterol 0.01 to 0.03; but in large white kidney: free 0.22 to 0.33 per cent., and ester cholesterol 0.09 to 0.65 per cent. Fex obtained similar results, showing that in cases of glomerular nephritis and of nephrosis the free cholesterol is hardly if at all increased, but the ester is greatly increased. He also found the liver and suprarenals in these cases were normal.

In a case of advanced chronic glomerulo-nephritis we found that, though the blood cholesterol was normal, the kidney was abnormally rich in ester: free 0.27 per cent., ester 0.2 per cent. In another case in which high hypercholesterolaemia had been noted a few months before death the kidney contained free 0.39 per cent. and ester 0.36 per cent. The analysis of other organs—liver, lung, spleen—was approximately within normal limits.

MYXOEDEMA

The total cholesterol of plasma in this condition may be increased by nearly 50 per cent. above normal. Epstein and Lander thought that blood cholesterol was inversely proportional to the basal metabolic rate, and they suggested an analogy between myxoedema and pure "nephrosis," where the basal metabolic ratio is also below normal. This argument was then used to explain the occasional beneficial results of thyroid medication in "nephrosis." However, Gainsborough and I found that this relation of basal metabolic rate and blood cholesterol does not exist in states of hyperthyroidism where, as in exophthalmic goitre, the blood cholesterol is within normal limits.

It may be thought that I have laid too much stress on the chemical aspects of the problems of sterol metabolism. Another method of approach, however, to these problems—in some aspects just as important—is afforded by the histological study of pathological conditions in which deposits of cholesterol esters occur in the tissues, as in chronic nephritis, Niemann's disease, atherosclerosis and in xanthoma. In some of these the deposition of sterol is apparently not determined so much by a hypercholesterolaemia as by the local lesion, whatever may be its nature, as in atherosclerosis. In other cases the deposits seem definitely due to an increase in blood sterol. The contrast is well seen in cases of xanthoma. In xanthoma simplex the lesion is unassociated with hypercholesterolaemia. On the other hand, the hypercholesterolaemia in prolonged jaundice may lead to a widespread distribution of xanthomatous lesions, and that in diabetes may lead to a differently distributed but characteristic xanthoma eruption, whereas the high blood cholesterol of so-called nephrosis never, so far as I am aware, leads to such phenomena.

ATTENUATION AND PREVENTION OF MEASLES *

BY

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The subject which has been chosen for discussion to-day is ripe for consideration on practical lines. On the one hand we have a disease responsible for a large loss of life and much permanent disability among that section of the population that has been the subject of special solicitude from public health authorities. On the other hand research promises that if certain difficulties can be overcome the ravages of measles might be greatly curtailed.

We have been in possession of the requisite knowledge for several years, yet very little effort has been made—in this country at least—to apply it. The difficulties of applying it are real and formidable, but it is high time that an influential body of hygienists, such as that represented by the present meeting, should get together and decide what ought to be done. Fortunately the speakers who will follow me will be able to report that a start has already been made, and they will be able to inform you of schemes of measles prophylaxis which are in actual operation. In these circumstances I think I can best serve the purposes of the discussion by referring to some of the more general problems, leaving it to others to describe in detail their own work and the successes and difficulties with which they have met.

Aetiology of Measles

The first step in the prophylaxis of an infectious disease should be some knowledge of its aetiology, and of the aetiology of measles we know next to nothing. It is invidious, but necessary, to discount the great majority of observations which have been made on this subject. There have been recurrent claims that measles is due to a visible bacterium. The most recent of these have been by Caronia, who has isolated a small Gram-negative coccus; by Tunnicliff, who implicates a green-producing streptococcus; and by Ferry and Fisher, who state they have isolated a similar streptococcus which, they assert, produces a potent toxin. All three claims have been challenged by a majority of workers who have attempted to substantiate them, and I think it is quite fair to state that they have carried no conviction to bacteriologists in general.

In the absence of any clear evidence that measles is a bacterial disease it is customary to consider it as due to an ultra-microscopic virus. For this view there is a considerable amount of support, both direct and indirect. The high infectiousness of measles without any concomitant bacteriological findings, the long "silent" period of incubation, the nature of its exanthem, its rapid evolution and devolution, its great constancy of clinical aspect, and the consistent and lasting immunity conferred by an attack—all these point to a relation with a "virus" rather than with a bacterial disease.

The direct evidence that measles is due to a filterable virus, though perhaps not so solid as the importance of the subject demands, is none the less weighty. In the first place, the only experimental animal which has been shown at all convincingly to be susceptible to the disease is the monkey. Hektoen and Degkwitz have amply confirmed the results of earlier and less controlled experiments, going back to the time of Francis Home, that the blood of cases of measles in the early stage of this rash is infectious to children. But even here natural infection seems to be much more certain than any artificial method. Regarding the susceptibility of monkeys results have been conflicting, and though Blake and Trask have brought forward very convincing evidence of the susceptibility of *Macacus rhesus* I imagine that few bacteriologists would look upon their demonstration as a closed chapter. Perhaps the most important point in their work is that they appear to have demonstrated that Berkefeld N filtrates of nasopharyngeal washings could produce the disease in monkeys. In monkeys Blake and Trask observed, after an incubation period of six to ten days, conjunctivitis and a macular eruption, accompanied by a leucopenia, and followed by an immunity to further inoculation. It is to be regretted that at the time of Blake and Trask's experiments knowledge of the serum prophylaxis of measles was not enough advanced to suggest to them the counter-check of attempting to prevent their disease in monkeys by previous inoculation with serum. This, had it come off, would have added considerable support to their observations.

Possibilities of Immune Serum

As no domestic animal appears to be susceptible to the disease the only source of immune serum against measles available is the human being who has passed through the disease.

It is to Nicolle and Conseil (1918) that we owe the first experiments suggesting the utility of this serum. Since then many other workers, particularly Debré in France and Degkwitz in Germany, have worked out the details of the method of prophylaxis, the latter initiating the inquiry as to the value of serum taken from adults who have had measles in infancy. As to the value of serum taken in early convalescence, there is a very general agreement among workers throughout the world, many of whom have claimed 80 to 90 per cent. of successes if the serum is properly administered. But it would be unfair to suppress the fact that breakdowns are often met with, due sometimes to factors that are readily explicable but not infrequently occurring when no such explanations are forthcoming.

It is of course very difficult to collect conclusive facts on such a method of prophylaxis as this, and highly infectious as measles is, everyone meets with extraordinary vagaries in its infectiousness. Certainly individual successes in prophylaxis prove nothing. One must remember that remarkable results have been recorded using antibacterial serum and even normal horse serum. It is the cumulative experience derived from many efforts carried out all over the world that persuades us that convalescent serum is a really effective prophylactic reagent.

Practical Aspects

The use of convalescent serum is a procedure of very limited application, and whether the serum prophylaxis of measles is to be established as a practical public health measure will depend very much on the efficiency of serum taken from subjects who have once had measles. This I will call "adult," in contradistinction to "convalescent," serum. The published evidence in favour of its use has not up to now been convincing in all instances, though perhaps to-day we shall hear of valuable additions to this evidence.

Theory as well as experience, so far as it goes, suggests that serum is best collected immediately after the period of defervescence, for at this time such circulating antibody as is present is probably at a maximum. It is not to be supposed that this maximum is maintained

* Read in opening a discussion in the Section of Public Health at the Centenary Meeting of the British Medical Association, London, 1932.

for long. Our available knowledge of the rate of disappearance of circulating antibodies is largely based on studies of diphtheria antitoxin and of precipitin. In both these cases the maximum of circulating antibody is only maintained for a short period, and in the absence of further antigenic stimuli the amount of antibody in the blood soon falls to a small fraction of its original titre. A single antigenic stimulus given to a reactive child may cause the diphtheria antitoxin in the blood to reach 50 units per c.cm. a couple of weeks after the injection. Five weeks later the amount of antitoxin present may be only about a quarter of that amount (Jensen). If the protective antibody in measles follows even approximately the usual formulae of disappearance it is obvious that within a year or two of the attack the antibody remaining in the blood will be negligible, and one would imagine that it would need at least ten times as much adult serum as convalescent serum to serve for prophylactic purposes—namely, 50 to 100 c.cm. ; clearly an impracticable dose. It is important, I think, that this theoretical objection be answered by particularly hard facts, if indeed it can be answered at all. There is, however, at least a prima facie case that adult serum is of use, and I hope that to-day we will hear more evidence in its support, for the practical applicability of the serum prophylaxis of measles will depend largely on a favourable answer to this question.

Problem of Supply

The immediate problem is the admittedly difficult one of collecting a sufficient quantity of adult serum for an extensive and scientific trial. Dr. Gunn will tell us how far the London County Council has advanced in this direction, but it is obvious that this body will not be able to satisfy more than its own domestic needs, which are very great. The collection of serum must be made on a much larger scale if we are going to have enough to go round—even for trial. We badly need a central organization to further this work. Young volunteers prepared to part with their blood are perhaps not easy to find, but if more serum has not been collected in this country it cannot lightly be blamed on the public, among whom there are always plenty of generous-spirited individuals, so much as upon the medical profession, which has as yet done very little to organize the service and make the public aware of its necessities.

A Public Serum Service?

With the support of the Medical Research Council and the Ministry of Health, and with the co-operation of the London County Council, we have already started a small-scale volunteer service of serum donors among the students of University College and of University College Hospital Medical School, and we have no reason as yet to think that there is likely to be a failure of a steady flow of volunteers. The difficulty up to now has not been in finding volunteers, but in making use of them.

The removal of 200 to 300 c.cm. of blood from healthy young adults, far from doing any harm, has often been stated by the donor to be a tonic experience. The main practical problem is to remove the blood expeditiously and without pain or inconvenience. Our own experience of blood-letting has convinced us that there is room for improvement in the apparatus generally used for this purpose.

We have devised a simple blood-letting apparatus which we have found useful. The special advantages which we think this apparatus possesses are that it can be used by a single-handed operator and that the serum can be kept sterile and easily removed from the clot. We always use novocain as a local anaesthetic. If apparatus and operator allow serum to be collected without any hitch I see no reason why volunteers should not be almost unlimited. If a proper appeal were made to the right elements of the public the service might be almost indefinitely enlarged, and, if experience supports the use of " adult " serum, might be put on a permanent basis. One need only mention a few of the organizations to which one would be unlikely to appeal in vain for volunteers—the Red Cross Society, St. John Ambulance Association, Boy Scouts, Y.M.C.A., etc.

I believe that if a scheme were put on foot it would soon justify the appointment of a whole-time medical officer, and until such an officer is provided the work is likely to go slowly, for the harvesting of serum on a large scale is not easy to fit in with other duties. There is also the problem of the further treatment of the serum. The preparation of serum on a large scale for human use is not a responsibility that anyone with experience is likely to underrate, and, under any scheme, would have to be allocated to a serum worker of special competence. Fatal accidents have already been reported abroad owing to the use of contaminated measles serum.

Proper Field of Application

If an organized supply of serum were arranged it is obvious that general practitioners and others would have to learn to use it conscientiously, for it would be unlikely that the available supply would suffice for any but urgent cases, such as the protection of sick and weakly children or the prevention of spread in hospital wards and other children's institutions. At least its use should be limited to children under 4 years of age, except in special instances, for not only does the risk to life become almost negligible after that age, but there are many indications that it is much more difficult to protect older children even with the most potent serum.

The family doctor may be faced with the awkward situation that the infant he has successfully protected may be exposed a couple of weeks later to an infection in an older brother or sister whom he has been unable to protect, for it is doubtful if passive immunity with ordinary doses of serum can be expected to last more than a few days. It is generally believed that an attack of measles may be attenuated by doses of serum not sufficiently great to prevent the disease, but that this is in any way a regular and easily controlled effect should, I think, be accepted with reserve pending the collection of more conclusive evidence. Trivial attacks of measles are common enough in uninoculated children, and a decision on the attenuating effects of serum is extremely difficult, particularly as allowance must always be made for the optimistic interpretation of pioneers.

There are two other points which I hope will be dealt with during the discussion: Is there any danger of the child who is apparently completely protected with serum being a source of infection to others? Is there any evidence that sterile human serum ever gives rise to local reactions when injected into children?

I have avoided putting forward any views as to the part public health authorities should play in the furtherance of these prophylactic schemes remembering that Burke says: " It generally argues some degree of natural impotence of mind or some want of knowledge of the world, to hazard plans of government except from a seat of authority." To-day we have a unique gathering of those " in authority " in the public health world, and not the least valuable part of this discussion should be their views on the practicability of a comprehensive scheme for the collection, distribution, and trial of prophylactic measles serum.

THE CHOICE OF AN ANAESTHETIC FOR ABDOMINAL SURGERY*

BY

Professor H. FINSTERER

VIENNA

Professor Finsterer said that the invitation to read an opening paper on the choice of an anaesthetic for abdominal surgery at the Centenary of the British Medical Association was the greatest honour ever conferred upon him.

He had sent a questionary to 200 members of the German Surgical Society, asking for their views and experiences, and had received 120 answers. His own experiences referred to 5,172 abdominal operations performed by him within twenty-five years under various methods of anaesthesia, and worked out statistically. In abdominal operations anaesthesia was of much higher importance than in any other operation, for in all acute diseases of the abdomen, as well as in chronic diseases of the gall-bladder and the stomach, the parenchymatous organs—most of all the liver—were already injured, so that further damage caused by general anaesthesia might be followed by death from insufficiency of the organs. As the protective ferments had been diminished, the danger of post-operative peritonitis and of consequent death was greater. Generally anaesthesia was regarded as dangerous only if the patient died during the operation. The frequency of these deaths from narcosis depended on whether all the fatalities during narcosis—even if they might have been caused by the grave disease itself—as well as all the cases where death occurred several hours after the operation when the patient did not awake from the narcosis, were still considered as being due to narcosis or not. By paying strict regard to the contraindications (severe heart or pulmonary diseases and other conditions) and by improving the technique of narcosis, the number of deaths from it had greatly decreased, so that they were scarcely to be feared. Of greater importance were the fatalities from late injury, which were connected more with the duration and depth of the narcosis than with its technique.

NARCOSIS

Chloroform caused most of the immediate deaths, even in small operations, especially at the beginning of the narcosis. It injured the parenchymatous organs, particularly the liver ; it regularly induced gastro-intestinal atony with frequent vomiting, often leading to death. Narcosis with ether was the most commonly used anaesthetic, administered either by the open or by the rebreathing method. To diminish the quantity of ether and to avoid the mucous secretion, as a pre-operative measure the patients received morphine or pantopon, together with atropine or scopolamine. Statistics from Austrian and German clinics showed that the immediate risks of ether were very slight. Of much greater importance were the so-called deaths from operative shock occurring three to five days after the operation, which were nearly always delayed anaesthetic deaths, as they did not occur when deep narcosis was avoided. They were caused by primary circulatory weakness with a poor distribution of blood due to injury by the anaesthetic and operative trauma (histamine effect). According to his experience the narcosis was of the highest importance, the operation itself, when delicately done, was of minor influence, because the weakness of circulation was absent when one operated under local anaesthesia. Some of the deaths were caused by injury to the liver, kidney, and the suprarenal gland. The researches of Bourne, Crile, and others had shown that prolonged ether narcosis produced injuries similar to those caused by chloroform. The liver was the most important regulative centre in metabolism, so that if it had been injured by acute or chronic disease the addition of ether narcosis resulted in a diminution of the alkali reserve and an increase of acidosis, owing to an insufficiency of the liver. Clinical tests of the liver function after ether narcosis demonstrated liver damage. In the material collected by him eighteen deaths from this cause were reported.

In his series of 610 operations under narcosis there were thirteen deaths from circulatory failure during the first five days. Of 122 stomach resections for ulcer seven patients died from this cause. Deaths from atony of the stomach after ether narcosis were rarer than after chloroform narcosis. They were due to a central paralysis of a common innervation centre for stomach and upper jejunum. Necropsy always showed that the stomach, duodenum, and upper jejunum were dilated to the utmost, and filled with liquid contents ; peritonitis was not present. Thirteen surgeons had reported thirty-four deaths from this cause, and he had observed five in 610 operations. He had had no deaths from atony after 4,562 operations under local anaesthesia.

Prolonged ether narcosis injured or destroyed the normal powers of resistance, especially phagocytosis, so that the smallest infection, insignificant in operations under local anaesthesia, led to death from peritonitis. In his clinic the mortality from peritonitis following gastric resection for ulcer was 4.4 per cent. under narcosis compared with 1.4 per cent. under local anaesthesia. Ether also favoured pneumonia by diminishing the resistance of the lungs, by chilling, by preventing expectoration, and by embolism. It was remarkable that in Nordmann's clinic the frequency of death from embolism rose from 1.4 per cent. to 4.4 per cent. when ether replaced chloroform. On the other hand, Sudeck had found that the substitution of nitrous oxide anaesthesia for ether anaesthesia diminished the frequency to one-tenth of the previous number. An increase of the coagulation of the blood had been observed after ether narcosis. The frequency of death from embolism in Professor Finsterer's clinic was higher after ether narcosis (0.98 per cent.) than after local anaesthesia (0.24 per cent.). Narcosis with nitrous oxide did not injure the parenchymatous organs, and was therefore the least dangerous. Fatalities were caused by technical mistakes. In protracted narcosis injuries of circulation seemed to be possible.

Avertin was being used by forty-five surgeons out of 120, mostly in selected cases. Its greatest advantage over general and local anaesthesia was that the mind of the patient was absolutely excluded. Specht calculated the frequency of unavoidable deaths from avertin as 1 in 10,000 ; deaths from gastro-intestinal atony were excluded, and the fatal cases were classified as avertin deaths by the authors themselves. The number of deaths could be restricted by using avertin as a basal hypnotic and by individual dosage, but unfortunately it could not quite be avoided. For this reason he did not use avertin as a basal hypnotic. Moreover, in many cases of basal hypnosis the amount of ether required was greater than when local anaesthesia of the abdominal walls and mesenteric anaesthesia were combined with ether narcosis.

Pernocton had been recommended for basal hypnosis, but the statistics of Bumm and others showed that this narcotic could not be called a harmless one. Seventeen surgeons had reported to him five deaths from pernocton.

* Abstract of a communication to the Section of Anaesthetics at the Centenary Meeting of the British Medical Association, London, 1932. The full text will be published in the *British Journal of Anaesthetics*.

Local Anaesthesia

Choice of Method

The sensibility of the patient was reduced by pantopon one hour before, and by morphine and atropine a quarter of an hour before, the operation. Professor Finsterer performed a regional or conductive anaesthesia by which the sensitive nerves were blocked within the abdominal wall, or in the mesenteries, or near the spinal column, or within the dural sac. In every laparotomy an exactly performed anaesthesia of the abdominal walls was most important. This applied also to paravertebral anaesthesia. It might also be added to spinal anaesthesia, for when the efficiency of the spinal anaesthetic had ceased the abdominal walls were still insensible. Anaesthesia of the abdominal walls was sufficient for gastrostomy, jejunostomy, colostomy, and also for gastro-enterostomy. In all other operations at least mesenteric anaesthesia procured by novocain was essential. This was absolutely without danger, prevented shock, and should therefore be applied to spare the general narcosis, even if this had been administered. When the organ was fixed the peritoneum of the posterior abdominal wall had also to be anaesthetized by paravertebral or splanchnic anaesthesia, or there might be used a short general narcosis.

Posterior splanchnic anaesthesia might be applied in every case, even in the presence of adhesions; fatalities due to intravenous or intraspinal injection could be avoided if the patient were in the sitting position. Kappis had no deaths in over 1,500 cases, and the results of other surgeons were equally favourable. Takats, however, reported from the literature 2,475 cases with eight deaths. Applying the criterion of Specht, previously mentioned, the mortality was 1 in 5,895. Professor Finsterer was now using anterior splanchnic anaesthesia if he planned to do a radical operation after exploratory laparotomy, injecting not more than 70 c.cm. of 1/2 per cent. novocain solution, with 1/4 per cent. solution in cachectic patients. In 115 out of 1,324 cases, general narcosis was used either to avoid pain during the introduction of the needle, or from the beginning at the request of the patient (the anaesthetic being withdrawn after the injection had been made), or for the separation of adhesions. He had collected 2,373 cases of anterior splanchnic anaesthesia without any fatality (British Medical Association Meeting, 1926) ; the number must now have reached at least 9,992. He had had one fatality due to injection of pantocaine which had been erroneously prepared (0.5 per cent. instead of 0.5 per thousand). This method procured in more than 90 per cent. of all his cases absolute anaesthesia for operations in the upper abdomen. It might be possible to obtain safe anaesthesia of the whole abdominal cavity by filling it with pantocaine.

Paravertebral anaesthesia had been used by him 174 times, mostly in resections of the large intestine, to mobilize the fixed colon ; for the resection, mesenteric anaesthesia was added. Parasacral anaesthesia was only sufficient for operations on the rectum and the perineum. Combined with a block of the hypogastric plexus it was sufficient for all hypogastric operations. Bürgkhardt reported over 1,000 cases without fatality ; Frigyesi 1,745. Professor Finsterer had had one death in 126 cases (due to severe haemorrhage).

Epidural (sacral) anaesthesia was sufficient for pelvic operations. By using the high Trendelenburg position and larger doses of novocain the anaesthesia could be extended as far as the dorsal segments. This method was not harmless.

Spinal anaesthesia had the great advantages of simple execution, of absolute painlessness, and of muscular relaxation. Its principal danger lay in the fall of blood pressure and in the endangering of the respiratory centre either by direct paralysis from the anaesthetic or probably in consequence of the lack of blood supply because of the depression of blood pressure. The higher the anaesthesia the greater the danger ; therefore few German surgeons (only fourteen out of 120) used high spinal anaesthesia. Pitkin declared that high anaesthesia with spinocain was the safest method, but his claims had not been substantiated. In operations below the umbilicus spinal anaesthesia was used by only forty-four of these surgeons. In order to prolong duration of anaesthesia percaine had been used. He had given up spinal anaesthesia fifteen years ago, and introduced combined parasacral anaesthesia, which was not only more safe but efficient for a longer time (two to three hours). If further experience should demonstrate that the efficiency of spinal anaesthesia could be protracted without increasing its risks—perhaps by employing pantocaine—he would again use spinal anaesthesia in operations on the lower abdomen.

Drugs and Comparative Mortality

The most commonly used drug for local anaesthesia was novocain in 1/2 to 1 per cent. solution combined with adrenaline. On the average 1 gram of novocain in 1/2 per cent. solution could be used without injury. Of the 1/4 per cent. solution much larger quantities (up to 500 c.cm.) could be applied without any symptoms of poisoning. In cachectic and anaemic patients 1/4 per cent. solution was absolutely sufficient. In aged patients with extreme arteriosclerosis it was advantageous to add pituitrin instead of adrenaline to the solution of novocain. Percaine was more poisonous and caused necrosis of the tissues ; he had had two deaths within twenty-four hours following its use. Local anaesthesia was almost without any immediate danger. In his series of 4,562 operations he had had only five deaths during operation or shortly after in spite of the high number of cases with bad risk. Two deaths were connected with the anaesthetic ; one had been already mentioned, the second was a real death from shock. Deaths within the first three to five days were exceedingly rare (0.08 per cent. compared with 2.2 per cent. in operation under narcosis) ; there were none from gastro-intestinal atony.

The mortality from pneumonia had been considerably reduced. In 610 operations under general narcosis it was 1.31 per cent. ; in 4,562 operations with local anaesthesia only 0.24 per cent. In 843 patients from 60 to 88 years of age, mortality was 0.94 per cent. only. In stomach resection for gastric or duodenal ulcer the death rate was, in 1,408 cases, 0.07 per cent. (one death in ninety cases under ether). In 510 operations for gall-stones he had had no death at all. As all cases, even those suffering from pulmonary disease, were operated on, a careful after-treatment (regular deep breathing, sufficient expectoration, injections of camphor oil, transpulmin) was important to avoid a fatal pneumonia. Serious disease of heart or lungs, extreme cachexia, old age, were no contraindication to an absolutely indicated operation. Nervousness, extreme adiposity, as well as infancy, were generally looked upon as contraindications to the use of local anaesthesia. In nervous patients the operation could be begun with general narcosis. In the adipose, local anaesthesia was very necessary, and because of the fatty heart it was essential to reduce general narcosis as much as possible. Combined anaesthesia was the safest method for them. In children local anaesthesia might also be used with success if narcosis had to be avoided owing to the presence of some general disease. In all cases of bad risk general narcosis meant high dangers.

Use in Particular Diseases

In 170 acute appendix operations under narcosis, including cases with diffuse peritonitis, the mortality was

10 per cent.; in 346 operations with local anaesthesia it was only 2 per cent.

In operations on the gall-bladder general narcosis was still preferred by most surgeons; if the patient demanded narcosis the operation was begun under nitrous oxide, while a regional anaesthesia of the abdominal wall and an injection of the hepato-duodenal ligament was made, or splanchnic anaesthesia was used. In all other patients the operation was begun under local anaesthesia of the abdominal wall and paravertebral or splanchnic anaesthesia added. In eighty-nine plain cholecystectomies under general narcosis there were seven fatalities (two from gastro-intestinal atony), whereas in 333 under local anaesthesia the mortality was 0.6 per cent. Cases of common duct obstruction were always operated on under local anaesthesia. There was no death from liver insufficiency.

In cases of acute intestinal obstruction deep narcosis lowered the blood pressure, and therefore easily caused collapse, while the intestinal paralysis was increased. Spinal anaesthesia counteracted intestinal paralysis, and had been recommended for the treatment of ileus, but it produced a dangerous fall in blood pressure. In every case he opened the abdomen under local anaesthesia and used a short ether narcosis at the moment of searching for the obstruction; the further operation was done under local anaesthesia. In all cases the blood pressure was raised by pituitrin and intravenous saline infusion immediately before operation. The mortality was much less (116 cases, 16.3 per cent.) than in hospitals where general narcosis was the method of choice. The statistics he had collected proved this statement.

In resection of the stomach local anaesthesia and mesenteric anaesthesia, splanchnic anaesthesia, or basal hypnosis, were replacing general narcosis. In resection for cancer he had used splanchnic anaesthesia in 273 cases, mesenteric anaesthesia in 148. In some of these cases small quantities of ether were given besides. The mortality was much less under local anaesthesia; this was true also of resections of the stomach for ulcer, and of the radical operation for gastro-jejunal ulcer. In 134 patients between 60 and 78 years of age operated on under local anaesthesia three had died (2.2 per cent.), whilst in 1,196 younger patients the mortality was 4.1 per cent.

In resection of the colon general narcosis was still regarded as the method of choice; some surgeons operated under spinal anaesthesia. He himself operated exclusively with local anaesthesia, and applied, when mobilizing the colon, either a short ether narcosis or paravertebral anaesthesia. No post-anaesthetic atony had been observed which would cause leakage of the suture by over-dilatation. With local anaesthesia the results of the operation could be considerably improved. If the bowel were sufficiently evacuated one-stage resection of the left colon could be performed. In resection of the colon for tuberculosis, megacolon, colitis, etc., results of the one-stage resection were good (ninety-seven resections with three fatalities). Also in the operation for cancer the one-stage resection, even of the left side of the colon, might be done if the bowel were empty. His mortality in forty-one one-stage resections was 11.9 per cent., whilst Nordmann reported a mortality of 28 per cent. with general narcosis. By using local anaesthesia he could operate with success on highly advanced cases which had already been refused operation by other surgeons who preferred general anaesthesia.

Abdomino-sacral resections of a high cancer of the rectum had a high mortality from shock and infection. Up till 1922 he performed that operation under general narcosis with a mortality of 31 per cent. Since then he had operated under combined parasacral anaesthesia. Mortality was reduced to 15.7 per cent. in fifty-seven cases.

ORAL CHOLECYSTOGRAPHY: THE CUMULATIVE METHOD

BY

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Cholecystography has now taken its place as a routine method of examination in cases where the biliary system is thought to be at fault. The test consists in the giving, either by the mouth or by intravenous injection, of a medium, generally known as "the dye," which is opaque to *x* rays when concentrated in the gall-bladder.

Some Fallacies

Inability to obtain a shadow is, as a rule, a sign of improper function, the most usual cause of which is gall-bladder disease, past or present. Most radiologists will agree, however, "that the gall-bladder may not be visualized even after the intravenous injection of the dye in certain conditions in which there is no reason to suppose that the organ is actually the seat of disease."[1] Simple enlargement of the liver, malignant growth in the right upper quadrant of the abdomen, pregnancy in its later months, perforated duodenal ulcer, acute disease (general or abdominal), and temporary kinking of the cystic duct are some of the conditions likely to produce this somewhat contradictory result. Again, the gall-bladder shadow may be late in appearing, and in consequence may be missed. Graham regards this as being due to any parenchymatous condition of the liver which retards the excretion of dye.[1] Further, in 1928, W. W. Boardman[2] pointed out that it was possible for a gall-bladder not to fill at a first test, and to give a good shadow some weeks or months later although conditions had remained unchanged in the interval. This observation has been noted by others.

The position is, then, that a gall-bladder which is not producing symptoms may fail to fill or may give no shadow at one time and show a normal one later. "Non-filling" is generally recognized as the most important indication of gall-bladder disease, but it is also a sign which presents a definite margin of error, and, unless this point is borne in mind, mistakes in interpretation may arise. It is for this reason that one of us (J. H. A.) has advocated persistently the consideration of the case as a whole before surgery is advised, together with the repetition of the test in all doubtful cases,[3,4] a contention strongly supported by B. R. Kirklin in a recent paper.[5] How and when should the test be repeated? Rolleston and McNee[6] hold that "failure to fill" after oral administration of the dye "indicates merely the . . . necessity of an intravenous test." With this we cannot agree.

Advantages of Cumulative Test

Early in 1929, when testing keraphen (the form of dye used at Ruthin Castle), it was found, in a supposedly normal case, that the gall-bladder did not fill at the first attempt. When the test was repeated forty-eight hours later a good shadow resulted. Last year Sandström[7] described a new method for giving the dye in oral cholecystography. He argued that as the contrast medium,

owing to its slow elimination, is held in circulation for some time, a cumulative effect can be obtained if the dye be given in divided doses. In a relatively large number of cases in which by the old method no filling at all, or only a thin shadow difficult to interpret was obtained, renewed examination resulted in a much better contrast filling—thus establishing the diagnosis. This paper, coupled with our own experience, led to a modification of our routine procedure, which is now as follows:

The usual dose of dye, graduated to the size of the patient, is given by the mouth at 8 p.m., and the first radiograph is taken at 8 o'clock the next morning. The film is examined as soon as possible, and, if the gall-bladder has failed to fill or has filled so poorly as to call for a repeated test, a special breakfast is given, omitting yolk of eggs in any form and reducing the fats. The same precautions are observed at lunch and tea, and at 8 p.m. the test is repeated, three-quarters of the previous amount of dye being used. In addition, 5 grains of Dover's powder are given an hour after the dye on each night.

In the last hundred cholecystographies the cumulative test has been done eleven times, and the results may be summarized as follows. Of nine cases which did not fill at the first test, two did not fill at the repeated test, three filled poorly, and four filled well; in addition, suspicious shadows were seen in three cases and a bilocular gall-bladder in one after the cumulative filling. Of the two cases which filled poorly at the first test one filled poorly the second time and the other gave a good shadow. The series included six men and five women, their ages varying from 29 to 73 years. Fuller details are set out below.

Table of Results

Case No.	Screening	First test	Second test	Emptying	Remarks
1	Neg.	D.N.F.	F.W.	Slow	
2	Faint Shadow	D.N.F.	F.P. Ringlets	Normal	Tender over gall-bladder
3	Neg.	D.N.F.	F.W. Ringlets	Normal	Attacks of pain right hypochondrium with fever and vomiting
4	Neg.	D.N.F.	D.N.F.	—	Intermittent light jaundice, bile in urine
5	Neg.	F.P.	F.W.	Normal	Attacks of pain in right hypochondrium with sweating
6	Neg.	F.P.	F.P.	Slow	
7	Neg.	D.N.F.	F.W.	Slow	
8	Neg.	D.N.F.	F.P. Ringlets	Slow	
9	Neg.	D.N.F.	D.N.F.	—	Intermittent nausea and flatulence
10	Neg.	D.N.F.	F.P.	Normal	History of jaundice. Pain and tenderness in gall-bladder region
11	Neg.	D.N.F.	F.W. Bilocular gall-bladder	Slow	Stools light-coloured

D.N.F. = Did not fill. F.W. = Filled well. F.P. = Filled poorly.

SUMMARY

1. There are certain dangers in regarding as pathological a gall-bladder which fails to give a shadow after a single cholecystography, oral or intravenous.

2. Eleven cases are quoted in which cumulative filling by the oral route was carried out.

3. The method employed gave added diagnostic information, and did not increase the reaction on the part of the patient.

REFERENCES

[1] Graham, E. A., Cole, W. H., Copher, G. H., and Moore, S.: *Diseases of the Gall-bladder and Bile Ducts*, 1929, London, Ballière, Tindall and Cox.
[2] Boardman, W. W.: *Amer. Journ. Med. Sci.*, September, 1928, p. 383.
[3] Anderson, J. H.: *Clinical Interpretation of Aids to Diagnosis*, vol. i, 1930, London, The Lancet, Ltd.
[4] Idem: *Medical Annual*, 1930, Bristol, John Wright and Sons, Ltd.
[5] Kirklin, B. R.: *Amer. Journ. Roentgen.*, May, 1931, p. 595.
[6] Rolleston, Sir Humphry, and McNee, J. W.: *Diseases of the Liver, Gall-bladder and Bile Ducts*, 1929, London, Macmillan and Co., Ltd.
[7] Sandström, Carl; *Acta Radiologica*, 1931, xii, 8.

Memoranda

MEDICAL, SURGICAL, OBSTETRICAL

MODIFICATIONS OF LINE RATION DIABETIC DIET

As the above diet is fairly widely used in this country it seems advisable to mention certain changes now introduced in the direction of increasing the carbohydrate. When the scheme was first introduced in 1924, the carbohydrate was high in comparison with other diets of that time. Since then the general tendency has been to increase carbohydrate, especially in insulin cases, and I have done so in my practice by prescribing more carbohydrate portions than protein and fat portions. The present modification introduces this change without affecting the essentials of the scheme.[1]

The carbohydrate content of each portion has been doubled, so that each Line now contains 10 instead of 5 grams of carbohydrate. The protein and fat of the Red portions have been kept the same. The factors by which the desired number of calories is obtained are slightly changed. Also several vegetables which used to be weighed have been included among the list of "negligible carbohydrate" content, as they do not contain enough starch to upset the balance between the rest of the carbohydrate, now raised in amount, and the insulin. This "negligible carbohydrate" is likely to amount to some 10 to 15 grams carbohydrate per day spread over the various meals. Although the carbohydrate prescribed has been increased, this has not been raised to the high amounts (200 or 300 grams) sometimes used nowadays. If really high carbohydrate diets seem desirable, the present scheme can be used by prescribing more carbohydrate (Black) than protein and fat (Red) portions. Where it seems advisable to add carbohydrate without increasing calories, the latter can be kept the same by cutting out 1/2 oz. of fat for each three Black portions added. In cases where it is more suitable to continue diets containing the lower carbohydrate of the previous scheme, this can be done by prescribing half or fewer Black than Red portions.

The examples and recipes in *The Diabetic A B C*[2] have been revised to conform with the above changes.

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HERPES ZOSTER AND VARICELLA IN THE TROPICS

The relation between herpes zoster and varicella is a very interesting one and recently much attention has been focused on this subject. The available evidence has been well summarized by Brain.[3]

In the British Solomon Islands I have recently come across two examples of cases of herpes giving rise to cases of varicella. There are two factors which lend interest to the study of the epidemiology of any infectious disease in an isolated place like this. In the first place we have a small population scattered over many different small islands, and the route of infection in any given epidemic is usually easy to trace. In the second place we are dealing with a population which has not acquired any immunity to our common diseases during childhood. During five years' residence here I have seen epidemics of measles, acute poliomyelitis, whooping-cough, and varicella. In all epidemics except whooping-cough the adults

[1] *The Line Ration Scheme*. Messrs. Lewis and Co., 1932.
[2] *The Diabetic A B C*. Messrs. Lewis and Co., 1932.
[3] Brain, W. Russell: "Zoster, Varicella and Encephalitis," *British Medical Journal*, 1931, i, 81.

seemed to be more susceptible to infection than the children.

Obviously, under such conditions one has quite unusual opportunities of studying our common infectious diseases in a susceptible race, and the following observations on the relation between herpes and varicella have been thought worth putting on record. The work has been done at a small hospital on the island of Vella Lavella in the Western Solomon Islands. The patients are all typical Melanesians.

On the evening of September 3rd, 1931, one of my "house-boys," a Solomon Islander of about 14 years of age, reported sick, complaining of a headache and general malaise. His temperature was 101° F. He was provisionally diagnosed as suffering from malaria and admitted to hospital. His blood film was negative for malaria parasites, but as he had been taking prophylactic quinine this was not considered significant. On the morning of the 5th a definite vesicular rash appeared on his face and forehead, well-marked vesicles being also seen on the nasal septum, the palate, and the uvula. A tentative diagnosis of varicella was made and the patient isolated. A generalized rash followed and the patient ran the normal course of a rather severe case of chicken-pox. The question immediately arose as to the source of infection. There had been no epidemic of varicella in the district for some years, and the closest investigation failed to reveal any other cases on the island from which the patient could have been infected. His record showed, however, that from August 14th to 17th he had been in hospital with a slight sprain of the right ankle. During this time he was in close contact with a severe case of herpes zoster. This case was a man about 35 years of age with herpes involving the twelfth dorsal and the first lumbar areas on the right side. I had noted on his record card that the vesicles were particularly bad on August 17th—that is, the day on which the boy was discharged. Inquiries revealed that at night time the boy often sat on the bed and talked to the patient with herpes.

It seems to me a reasonable inference that the boy contracted his chicken-pox from this patient. His own illness followed seventeen days after discharge.

The further history is interesting. From his admission on September 3rd until the appearance of the rash on the 5th the patient was nursed in a small ward with three other natives. These three men were immediately removed when our suspicions were aroused—that is, on September 5th. On September 21st one of these men and two hospital orderlies who had nursed the boy reported sick with a commencing chicken-pox eruption. The two other men who had been in the ward developed the same disease on the 22nd and 23rd respectively. All were male adults and all ran quite a severe course.

We subsequently had six more cases—the final case reporting on November 27th, 1931. The ages of the cases were roughly 14, 28, 23, 21, 42, 30, 9, 18, 21, 18, 21, and 25.

On March 5th, 1932, a neighbouring planter, who lives one mile from the hospital, came to see me complaining of severe pain in the right lumbar region and a rash over the same area. Examination showed severe herpes in the right lumbar region extending round the right side of the abdomen. He was sent home to bed and had a very painful and prolonged illness. On March 21st he noticed that his native house-boy, 16 years of age, who made his bed and attended to him personally, had a rash on his face, and he sent him over to hospital. He had typical chicken-pox of the usual degree of severity seen here. No cases of varicella had been seen on the island for over three months. The period from the commencement of his master's herpes till the beginning of his own illness was about eighteen days. Here again the connexion between the two cases seems to me to be clearly established. No further cases have arisen.

The deduction of practical value from our experience recorded above seems to be that unquestionably all cases of herpes occurring in native races should be rigorously isolated.

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A CASE OF MALIGNANT THYMOMA

The following are particulars of an interesting case which was admitted to Kirklandside Isolation Hospital early this year.

HISTORY OF CASE

On January 21st a male child, aged 2½ years, was admitted as a case of laryngeal diphtheria. The history was that he had not been very well for a fortnight, and had had a sudden attack of difficulty in breathing. The diagnosis before admission was thought by the family doctor to lie between laryngeal diphtheria and foreign body—probably the former.

On admission respirations were rapid and laboured; there was slight rib retraction; the colour and pulse were good. There was no membrane on the fauces, but the condition generally resembled that of a case of ordinary laryngeal diphtheria. The child was given 18,000 units of anti-diphtheritic serum intramuscularly, put in a steam tent, and given an emetic emulsion. He appeared to be fairly comfortable after treatment. On the next day (January 22nd) an additional 6,000 units of serum were injected; the child remained fairly comfortable. On January 23rd there was still some slight difficulty with breathing, but the child's general condition was good. During the three succeeding days steam was discontinued, the child appeared fairly comfortable, and the throat swab was negative. The child at this time was thought to be well on the road to recovery.

On January 27th the child had a spasm at 8.45 a.m., which lasted fifteen minutes. The respirations were laboured, the child was cyanosed, and was put in a steam tent again. On January 28th another culture was negative, and in the afternoon of that day another spasm, lasting fifteen minutes, took place. On January 29th the left lung appeared to be solid; breath sounds were distinct and tubular, but the child did not appear to be acutely ill. He slept well on the night of the 29th. On January 30th, in the afternoon, there was another spasm. On January 31st there were two spasms. On February 1st there was a spasm in the morning, which seemed to yield to a few minims of adrenaline. On the evening of that day Dr. Brand of Glasgow was called in to see the case. The chest condition was the same as on January 29th. The larynx was examined, but nothing definite was found. A spasm occurred when Dr. Brand was examining, and seemed to yield to a few minims of adrenaline. A provisional diagnosis of spasmodic asthma was made on the case, but the chest condition was still not clear. On February 3rd the child was removed to the Victoria Infirmary, Glasgow.

The urine during the whole time was clear, and only on one occasion, January 29th, did the temperature rise above normal.

On February 4th a diagnosis of pleural effusion and thymic asthma was made, and the left side of the chest was aspirated. A quantity of turbid pseudo-chylous fluid was withdrawn, which was found to contain large numbers of lymphocytes; no organisms were found on direct examination or on culture. After the thoracocentesis the child improved, but about two days later began to have severe laryngeal spasms, and became very blue. Tracheotomy was performed, but the child died.

POST-MORTEM FINDINGS

The thymus was greatly enlarged and replaced by a potato-like tumour, which extended down and completely filled the anterior mediastinum. It surrounded the heart, great vessels, trachea, and oesophagus, and displaced the heart backwards. The mass was the size of a small melon. The left lung was collapsed and adherent to the tumour, and its pleural cavity was filled with the grey turbid fluid described above. The tumour had extended outwards from the hilus of the lung underneath the pleura, along the lines of the ribs from the second to the tenth. The right lung was normal. No other organ was involved except the kidneys, which were enlarged and nodular, and contained masses of tumour tissue resembling the thymic tumour. The mediastinal and inferior deep cervical glands were involved. The spleen contained excess lymphoid tissue. Pathologist's diagnosis: malignant thymoma.

I am indebted to Dr. W. Bell for sending me particulars of the case whilst in the Victoria Infirmary, Glasgow, and for the pathologist's report.

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Reviews

CELLULAR PATHOLOGY OF THE NERVOUS SYSTEM

In the monographs which comprise *Cytology and Cellular Pathology of the Nervous System*,[1] Professor WILDER PENFIELD has provided a contribution to medical literature which will be welcome to neurologists and pathologists alike. Though it will be a matter of regret to readers in this country that in a work derived from so many sources only one article is written from an English school of medicine, the editor has had at his command the experience of the best authorities in Europe and America. The volumes are fittingly dedicated to the "Spirit of Scientific Investigation . . . of Ramón y Cajal," and an outstanding reminder emerges from them that medical science owes an enormous debt to this pioneer of histological investigation. In the present work perhaps the most valuable contributions are made by pupils of this Master's school. As might be anticipated, the freedom which has been given to each author to present his subject according to personal views has brought shortcomings as well as advantages. It is inevitable in a subject in which such rapid growth is taking place that there should be the expression of divergent views a little confusing to the reader. Thus, in Section XI the production of cerebro-spinal fluid is regarded as a process of secretion, and in Section XII as one of dialysis. The space devoted to the various subjects also suffers in places from a lack of proportion. In a work of 1,255 pages no fewer than 66 are devoted to the pineal body and 35 to the vermiform appendix, whereas only 40 are given to the subject of nerve endings in the blood vessels and viscera, and 35 to the blood vessels of the brain and cord. In compensation for these disadvantages there is a wealth of detail which could only come from personal experience, and which would suffer were the authors less free to follow their own inclinations.

The volumes are attractively produced, well bound, and well documented, but though we have become accustomed to a bewildering profusion of new names in neuropathology, there is no excuse for such atrocities as "schwanoid" or "piloid," even though the derivation is naïvely appended as from *pilus* (a hair) and *oides* (like)! The illustrations are an outstanding feature, and if one were to offer any criticism of them it would be of their profusion rather than of their quality. Vol. i deals mainly with the cytology of the peripheral nervous system. It opens with a section on the general characters of the neurone by Cowdry, which consists chiefly of a critical review of recent advances in the knowledge of the minute structure of the nerve cell, with indications of the lines upon which further progress is likely to be made. This and the following section on the development of the nervous system will both appeal to the specialist rather than to the general reader. De Castro's chapters on the sensory and sympathetic ganglia, and Boeke's on sensory and motor nerve endings, are particularly valuable. An excellent descriptive account of these structures is given with numerous good illustrations, which give a far clearer conception of the connexion between the conducting and effector apparatus than has hitherto been available, and one regrets that the scope of the work prevents any discussion on the physiological problems which arise. Vol. ii is devoted to the minute structure of the brain and its derivatives and membranes. Del Rio-Hortega contributes an interesting section on microglia. Cobb, in a chapter on the blood vessels, exposes the time-honoured fallacy that the brain is an organ supplied by end-arteries, and sets forth evidence, both from intra-vitam methods in animals and investigations on human post-mortem material, that the cerebral vascular supply forms a continuous network—a theory more in accordance with clinical experience than that usually taught. He considers the Virchow-Robin space to be a definite persistent structure round the larger vessels, continuous with the subarachnoid space on the one hand, and with a variable potential space round the finer vessels on the other. Vol. iii treats of the tumours and malformations of the nervous system. Bailey, in his section on gliomata, restates in a simplified form the classification set forth by himself and Cushing in 1926. Further changes in nomenclature are made. It is to be regretted that this already confused subject should be worse confounded for no better purpose than an attempt to fit observed facts into an over-rigid theory of the relation of tumour formation to embryological cell types, which, though it has served a useful purpose in stimulating thought and investigation, has already been shown to be inadequate as an explanation of the pathogenesis of tumours elsewhere. Penfield writes the section on tumours of nerve sheaths. He draws a clear and overdue distinction between the solitary tumours of the eighth nerve and spinal roots and the multiple tumours of von Recklinghausen's disease, which may give rise to growths in these same situations. The solitary perineural fibroblastoma is a tumour of mesodermal origin arising from the perineurium, the older views of Verocay (1910) and Masson (1923) that it arose from the sheath of Schwann being due to faulty staining methods. The von Recklinghausen tumour, on the other hand, is part of a general reaction of nervous structures, bones, and skin to some unknown influence, and they invariably contain true neurofibrils. The remaining sections on tumours are all adequate.

There can be no doubt that these volumes represent a valuable contribution to medical science, and with their full and discriminative bibliography will prove of lasting help to those who are interested in the study of neuropathology. For the clinical neurologist vol. iii is the most useful of the series.

[1] *Cytology and Cellular Pathology of the Nervous System.* Edited by Wilder Penfield. Vols. i, ii, and iii. New York: P. B. Hoeber, Inc. 1932. (Pp. 1,280; 886 figures. 30 dollars the three volumes.)

BLACKWATER FEVER

In a memoir of the London School of Hygiene and Tropical Medicine, entitled *Researches on Blackwater Fever in Southern Rhodesia*,[2] Dr. G. R. Ross gives an extensive report on the work done by him during four years of research in Southern Rhodesia. The memoir comprises 262 pages, with an index, and is divided into three sections, in which are discussed the epidemiology, the blood and urine, the chemical aspects, and the treatment of blackwater fever. Each section is accompanied by a list of references. The whole problem of blackwater fever is ably reviewed by the author in a most thorough and critical manner, and the memoir will thus form a very valuable work of reference to all those interested in this serious and puzzling malady.

In the section on epidemiology the writer has demonstrated graphically the correlation of the incidence of malaria and haemoglobinuric fever, and there seems to be little doubt but that malaria in some way or other is a necessary preliminary to the development of the susceptible state in which haemoglobinuria may occur. Apart from this sensitizing action on man malaria also plays

[2] *Researches on Blackwater Fever in Southern Rhodesia.* By G. R. Ross, M.B., Ch.B., Ph.D., D.P.H. No. 6 of the Memoir Series of the London School of Hygiene and Tropical Medicine. London: London School of Hygiene and Tropical Medicine. 1932. (Pp. vi + 262. 10s. 6d. cloth; 8s. paper.)

a part in the precipitation of the actual attack. The fatality rate averaged 22.2 per cent. in a total of 679 cases collected over a period of fifteen years. This percentage corresponds very closely to that of other observers. The fact that three cases of blackwater fever out of every four may be expected to recover is a point which must be taken into consideration in presenting evidence of the value of any particular line of treatment. This was emphasized by Thomson (1924), and Ross draws particular attention to this important truth, which is often overlooked by the enthusiastic clinician in assessing the value of his treatment. The statement of Daniels, (1900) that there was no form of treatment that had any effect on the duration of the haemolysis remains true to-day.

Ross discusses fully the various theories set forth to explain the sudden haemolysis, which is probably intravascular; but there seems to be no definite evidence which proves conclusively the real cause of the haemoglobinaemia. As regards the mechanism of suppression it is interesting to note that he does not consider the explanation given by Baker and Dodds entirely satisfactory, and prefers the original view of Yorke and Nauss (1911) that the precipitation of debris depends upon the concentration of the urine. This naturally raises the question of the value of alkaline treatment in preference to any other form of therapeutics which has copious diuresis as its object. In conclusion, a careful perusal of this memoir cannot fail to impress the reader with the fact that the mechanism of the production of the haemolysis in blackwater fever is still an unknown problem. Further, the real cause of suppression seems in doubt, and there is no known specific treatment which will prevent or arrest the haemolysis.

Fortunately, on epidemiological evidence the proof is quite conclusive that haemoglobinuric fever is a sequel to repeated attacks of subtertian malaria and is therefore a preventable condition.

RHEUMATOID ARTHRITIS AND ITS TREATMENT

Drs. VINCENT COATES and DELICATI[3] have investigated the clinical picture and biochemical deviations of one hundred consecutive cases of rheumatoid arthritis at the Mineral Water Hospital, founded nearly two hundred years ago at Bath. By this name they signify chronic polyarthritis of unknown origin, excluding from this category the metabolic, degenerative, and neuropathic forms of arthritis, although wisely admitting that cases of mixed origin often occur. Like other students of rheumatism, they are painfully impressed by the hopeless crippling that befalls a large proportion of these cases if early treatment is neglected. In a suggestive table showing an "elastic grouping" of joint diseases, rheumatoid, like gonorrhoeal and dysenteric, arthritis, is placed with the infective diseases, but not in general as a focal infection. All aetiological classifications are at present provisional, and dogmatic statements as to the causation of this insidious form of arthritis cannot be accepted. Its facile ascription to focal infection, for example, has led to unbalanced methods of practice.

The authors have done good service in again calling attention to the clinical picture of this particular type of disease and of its little-recognized *formes fruste*. Thus they find that pyrexia in some degree occurred in sixty-eight of the hundred cases; tachycardia in sixty-six; enlargement of the spleen in twenty-one; acceleration of the sedimentation rate in ninety-seven, with haemoglobin generally deficient; absence of free HCl in a test meal in twenty-two; and enlargement of the lymphatic glands in fifty-three. With them, as with others, rheumatoid arthritis is a systemic disease with reactions in the joints, commencing in the wrists and fingers in nearly 80 per cent. of cases. The very long inflammatory period is characteristic. In dealing with treatment the authors set forth four objectives which they regard as necessary in the systematic treatment of rheumatoid arthritis, and which must be definitely kept in view in a properly planned sequence. These are the increase of immunity, the adjustment of chemical and biochemical abnormalities, the stamping out of infection, and the elimination of noxious products. Naturally, in the handling of all chronic diseases the factors of treatment must be coterminous with the factors of causation. In regard to physical treatment, it is stated that sedative baths and ultra-violet rays are of great value in the early stages, and the pool bath at a later stage, for the restoration of movement in stiff joints, and calomel is praised for the elimination of toxins. The slogan of "perpetual motion" is very properly condemned: one free movement daily in a whirlpool bath is often sufficient. Some space is devoted to suggestions, with diagrams, for the relief of contraction and deformity of joints in the later stages of the disease.

In the compass of a few pages the authors have set forth the systemic and local treatment of rheumatoid arthritis as met with in a spa hospital. Unfortunately, in such hospitals the disease is usually in an advanced stage. The functional disturbances present in the early stages, and the reactions which take place under treatment by various forms of baths, have never been described, and would well repay an exhaustive study.

[3] *Rheumatoid Arthritis and its Treatment.* By Vincent Coates, M.C., M.D., M.R.C.P., and Leo Delicati, L.M.S.S.A. London: H. K. Lewis and Co., Ltd. 1931. (Pp. xiv + 114; 12 figures. 6s. net.)

"IMMUNITÉ—INTOLÉRANCE—BIOPHYLAXIE"

Immunological research has given us a multitude of facts, but they sometimes appear an ill-assorted collection, difficult to knit together in a well co-ordinated story. It is true that in the case of acquired immunity and anaphylaxis there is the common theme of antigen-antibody reaction, but in allergy and the hypersensitive states the role of specific antibody is not apparent, while in natural immunity we have to confess to an ignorance of many of the mechanisms which ensure the defence of the body. The assumption is often made that what holds true in the case of acquired immunity is probably true also of allied states like allergy and hypersensitiveness, even though the experimental proof of this eludes us. Dr. ARNAULT TZANCK, like many others, has felt dissatisfaction with this state of things, and in a book entitled *Immunité—Intolérance—Biophylaxie*[4] gives us the fruits of his endeavour to sort out the facts and reveal underlying principles. He advances no new all-embracing theory, but considers the various phenomena concerned with the resistance of an organism to the invasion of noxious principles, living and non-living, with the avowed object of clarifying our conceptions concerning immunity and so rendering further research more fruitful and placing immunotherapy on a more reasoned basis.

After reading the preface we anticipated something almost revolutionary because of the opposition which the author fears his views will receive from the orthodox school of immunologists. But it seems to us that he has merely restated many generally accepted points of view in rather different language. No one, we imagine, would quarrel with the distinction he draws between intoxication and intolerance—a point which is given a whole chapter to itself—and the term "biophylaxis," which is defined as "l'ensemble des mécanismes défensifs non spécifiques que l'organisme met en jeu pour assurer sa guerison," is surely nothing more than is implied by

[4] Paris: Masson et Cie. 1932. (Pp. 268. 35 fr.)

immunologists when they speak of the beneficial reactions evoked by non-specific therapy, such as protein shock. It may be convenient to have a word such as biophylaxis which embraces all these ideas, but it does not advance our knowledge of the phenomenon, and there is very real danger in coining words like this because only too many minds seem quite satisfied that everything is known about a phenomenon once a ticket has been attached. Dr. Tzanck argues that since true antibodies cannot be demonstrated in many hypersensitive states their underlying mechanism must be different, and this mechanism he finds to be "cell memory." Well, of course it is; but to ascribe a phenomenon to cell memory does not help us to understand it better, any more than our conceptions of allergy are clarified by saying "allergie c'est la vie," an expression which seems rather to have taken the author's fancy.

THE AIM OF DIAGNOSIS

The recent editions of KREHL's Pathological Physiology[5] and Diagnosis of Internal Diseases[6] differ from the previous editions in minor particulars only. In the former work a short chapter on subnormal temperatures has been added, with further details on inanition, vitamins, the glycogen content of the liver, the action of insulin, etc.—all rather in the nature of finishing touches than substantial alterations. The same applies to the Diagnosis of Internal Diseases. With regard to the latter work Krehl states that his aim was to expound the general principles of diagnosis as distinct from the special diagnosis of individual diseases. The nature of the distinction is not altogether clear, and Krehl himself admits that he has not succeeded in eliminating the special point of view; it is, in fact, prominent in almost all parts of the work, although not applied in sufficient detail to preclude the necessity of his recommending a reference to special textbooks for more complete information. Looked upon as a diagnostic method, however, Krehl's conception of a general diagnosis is excellent. Special diagnosis may be said to have as its aim the labelling of a disease with an appropriate name. General diagnosis, on the other hand, starts with Krehl's favourite conception of the living body as a whole, consisting of a complex of interrelated processes; the aim of a general diagnosis, in the presence of any given lesion, is to ascertain what modifications, direct or by way of compensatory action, occur in these processes as a result of the lesion. General diagnosis would therefore seem to consist in the application, in the case of individual diseases, of the principles expounded in Pathological Physiology. The two books must be read together; they both exhibit the freshness and originality that characterize all Krehl's writings.

NOTES ON BOOKS

Psychology and Medical Practice[7] is a pamphlet of some sixty pages in which the author, Dr. HOFFMAN, professor of psychiatry and neurology in the University of Tübingen, puts at the disposal of the general practitioner his wide experience of psychological ailments. There is no reference throughout the text to Freud or Jung or Adler; but the author, while expressing his indebtedness to many modern writers on psychopathology and on neurology, states that it is the Nietzschian psychology that has inspired his present work. Dr. Hoffmann's aim has been to assist the doctor in general practice to a fuller understanding of the motivation of neurotic symptoms, and thus to enable him better to treat neurotic ailments. He insists on the necessity of a psychological approach to such cases. The psychological disabilities commonly met with are fully discussed, and he sketches in the emotional background of the various anxiety states, hypochondria, and the maiming of personality brought about through worry and fretting and peevishness. The author has contrived to compress into these pages a surprising amount of information about the neuroses, and his advice regarding their management is practical.

A French handbook, Clinical Methods,[8] by Drs. H. CAILLOUX and M. BLANC, contains a thoroughly up-to-date account of the principal laboratory methods necessary for the practitioner. The methods are described under the headings of urine, blood, gastric juice, etc., and after each investigation follows a concise paragraph dealing with the interpretation of results. The various investigations suitable for different diseases are indicated at the end in an alphabetical list of maladies.

We have received the second volume of the Reports of the Hospital for Infectious Diseases, Madrid,[9] formerly known as the Hospital del Rey, of which the first volume was noticed by us on August 15th, 1931. In addition to hospital statistics, the volume contains thirty-five papers, five of which deal with tuberculosis, five with typhoid fever, and the rest with typhus, agranulocytosis, pneumonia, and other respiratory infections.

Special Cytology,[10] edited by E. V. COWDRY, appeared first in 1928, and was reviewed in these columns. A second edition has now been published, embodying new information which has since been obtained, and correcting, so far as necessary, certain articles in its predecessor. The work runs into three volumes, and deals carefully and comprehensively with the nature and function of the cells in all the various systems of the body. It is a useful reference book on the cytology of the organs.

The bird is a convenient laboratory animal for the study of spirochaetes, and it is from this point of view that KNOWLES, DAS GUPTA, and BASU have published a memoir, entitled *Studies in Avian Spirochaetosis*.[11] The booklet is divided into two parts: the first deals with the history of the subject, the second with their own observations. They believe that "granules" do not represent any phase in the life-cycle of the parasite, but that the organism persists as such during the passage through the tick. The monograph is well illustrated and documented, and forms a valuable addition to the literature of the subject.

Pistol v. Poleaxe[12] is an impartial and vivid—perhaps too vivid—description of the various methods of killing animals for food in civilized countries. It is entirely free from prejudice; in fact, its main fault, if it is a fault, lies in the wealth of corroborative evidence which the author has included. Methods of humane killing are now so numerous and so effective that it is to be regretted that the lead set by Scotland in the compulsory use of mechanical means of slaughter has not been more widely followed. Even more important, however, is the necessity for a more modern treatment of animals immediately before slaughter. This is a book which must be consulted by all who are interested in the subject.

[5] *Pathologische Physiologie*. By Dr. Ludolf Krehl. 14 Auflage. Berlin: F. C. W. Vogel. 1932. (Pp. xii + 716. R.M.39.60; Geb. R.M.42.)

[6] *Die Erkennung innerer Krankheiten*. By Dr. Ludolf Krehl. Zweite auflage. Berlin: F. C. W. Vogel. 1932. (Pp. viii + 197. R.M.12.80; Geb. R.M.14.80.)

[7] *Psychologie und Ärztliche Praxis*. Von Herm. F. Hoffmann. Berlin: S. Karger. 1932. (Pp. iv + 67. RM.2.80.)

[8] *Technique des Prélevements dans la pratique clinique. Interpretation des Resultats du Laboratoire. Les Feuillets du Laboratoire*. By Hubert Cailloux and Marcel Blanc. Paris: N. Maloine. 1932. (Pp. 209; 16 figures. 25 fr.)

[9] *Trabajos del Hospital Nacional de Enfermedades Infecciosas* (Antes Hospital del Rey). Volume ii (1930–31). Madrid: Editorial Paracelso. (Pp. xvi + 786; illustrated. 16 pesetas.)

[10] *Special Cytology*. Edited by Edmund V. Cowdry. Second edition. New York: P. B. Hoeber, Inc. 1932. (Pp. 1,838; 757 illustrations. 30 dols. the three volumes.)

[11] *Studies in Avian Spirochaetosis*, Parts I and II. By Lieut.-Colonel R. Knowles, I.M.S., Assistant Surgeon B. M. Das Gupta, L.M.P., and B. C. Basu, M.Sc. Indian Medical Research Memoirs, No. 22. Calcutta: Thacker, Spink and Co., Ltd. 1932. (Pp. 113; 11 plates. 8s. 3d.)

[12] *Pistol v. Poleaxe*. By Lettice Macnaghten. With a foreword by Viscount Lee of Fareham, and a preface by R. G. Linton, Ph.D., M.R.C.V.S. London: Chapman and Hall, Ltd. 1932. (Pp. xxiii + 577; 94 figures. 21s. net.)

KING EDWARD'S HOSPITAL FUND

WORK AND FINANCE OF THE LONDON HOSPITALS

The annual statistical review for 1931, recently published by King Edward's Hospital Fund for London,[1] again provides proof of the strength of the financial supports upon which the voluntary hospitals rest. Despite the adverse circumstances of the year, the total voluntary gifts to the maintenance of the London hospitals amounted to £1,763,000, which, though slightly less than in 1930, was more than in any other year out of the five covered by the review. Although there was some decrease in 1931 from the high figures of 1928 and 1929 in the amount received from the general body of subscribers and donors, this was more than set off by an increase in legacies. Including receipts for building and endowment, the total voluntary gifts in 1931 amounted to £2,416,000. "Receipts for services" again showed a satisfactory advance on previous figures, reaching a total of £1,400,000.

In 1931 the total income of the 142 London hospitals amounted to £3,811,000, the highest figure recorded, and an increase of £34,000 on the previous year. Notwithstanding an advance of £38,000 on the total running expenditure, due to progress in various directions, including the upkeep of 330 additional beds, the aggregate surplus of income over expenditure for the year 1931 was £76,000, against £80,000 in 1930. If the individual hospitals are taken separately, 1931 shows a marked improvement on 1930, there having been eighty-five hospitals with surpluses, against seventy-two in the previous year, and only fifty-seven with deficits, against seventy in the previous year. While no one can yet say what the position will be in 1932, the results of the last two years may justifiably inspire the hope that, if the public continues to recognize the value of its work, and of its special contribution to the hospital service, the prevailing depression need have no untoward effect upon the finances of the London voluntary hospitals as a whole during the present year. The soundness of the position in London at the beginning of the year is demonstrated by the figures given in the King's Fund review just published, and is thus described in its conclusion.

"In the reviews of the past year or two it has been pointed out that a study of the aggregate figures presented in the review demonstrates in no uncertain fashion two broad facts—namely:

"1. The work of the voluntary hospitals in London continues to grow not only in scale but also in quality as a result of the progress that has been made in curative medicine and surgery. The hospitals have thus been enabled to provide more and more effective treatment for a continually increasing number of the sick poor for whom they were originally founded, and who remain their first care. The advances in therapeutic knowledge and skill have inevitably led to demands from other sections of the community that they should not be debarred from the benefits of the progress, and the voluntary hospitals, in adapting themselves to the changing conditions brought about by the ever-developing co-ordination of social life in this age, have met the necessities of the case by enlarging their field of service, which now includes not only the indigent sick but also a large body of wage-earners who make substantial contributions either direct or through contributory schemes, and also persons of moderate means who are admitted to the private pay-beds.

"2. In the aggregate the receipts, including both voluntary gifts and patients' payments, have kept pace with the increased maintenance expenditure. The voluntary gifts to maintenance show a substantial increase in recent years, in addition to which large amounts have been received from this source to meet the heavy expenditure on schemes of extension and improvements or reconstruction at existing hospitals, as well as on buildings for new hospitals. This capital expenditure has been a marked feature of the post-war finance of the voluntary hospitals.

"The last year or two have been years of increasing financial pressure upon all members of the community, and not least upon those that give voluntary monetary support to the hospitals. The year 1931 in particular may well be regarded as having been a testing time alike for the strength of the financial support of the voluntary system and for the spirit and efficiency of its voluntary management. The latter part of the year, the period in which most of the hospitals expect to receive an important part of their voluntary income, saw the announcement of heavily increased taxation accompanied by fears of further imposts. Even the most optimistic supporters of the voluntary system feared that when the figures of 1931 were known they would reveal that the financial support of the system had been unable to carry the burden.

"The figures contained in this review give no ground for believing that these fears have been justified. After allowing for the fact that the receipts in 1930 from subscriptions and donations included an exceptional single payment to maintenance of £100,000 which had no counterpart in 1931, the receipts from this source show a decrease of only £5,000. Though the total for 1931, £970,000, falls a little below the one million level first reached in 1928 and maintained in the two following years, it is higher than the total for 1927 and very much higher than the average annual receipts, about £820,000, from these voluntary sources in the five-year period prior to 1927.

"In discussions on the future of the voluntary hospitals attention is too frequently directed solely to the voluntary source of their income, while too little is paid to the voluntary management, which, with the voluntary services of the honorary medical and surgical staff, forms the other characteristic feature of the system. It is not too much to say that the voluntary management is the king-pin of the whole structure of the voluntary hospital system. It may roughly be estimated that the membership of the committees of management of the 142 voluntary hospitals dealt with in this review includes some 3,000 persons, to say nothing of the whole army of volunteers who work on other committees and in numerous less formal ways. Any slackening of interest or any loss of efficiency on the part of these voluntary managers and other workers would inevitably be reflected not only in a falling income, but also in a decreased volume of work and in a loss of instructed public interest in hospital questions which would react on the spirit and character of the whole of the hospital service of the country. The figures for 1931 are proof, if proof were needed, that the continuous stress of the last two or three years has found the vitality of the voluntary system unimpaired, and justify the confidence that the community is determined to make considerable sacrifices both in money and in personal effort to maintain it in its full vigour."

[1] Statistical Review of the Work and Finance of the London Hospitals for 1931, 7, Walbrook, E. C.4. (1s. net.; 1s. 3d. post free.)

CANCER CONTROL IN AUSTRALIA

REPORT OF THIRD AUSTRALIAN CONFERENCE

Each year a conference of delegates from the various States of Australia is convened at Canberra by the Director-General of the Commonwealth Department of Health to review the progress made in the fight against cancer, and to co-ordinate the various activities. At the third of these conferences, last March, Dr. M. J. Holmes, a member of the staff of that Department, reported that the University of Sydney had allotted some of its responsibilities more definitely to hospitals. Thus the Royal Prince Alfred, the Sydney, and the St. Vincent Hospitals had accepted the charge of the administration of clinics where radium work was being carried on. The first-named institution had also taken over the control of the deep *x*-ray therapy department, and it was hoped that before long the St. Vincent Hospital would be able to act similarly. The University would, however, maintain its general superintendence over treatment and retain its other responsibilities to the Commonwealth Government, providing grants in aid of treatment, and promoting reorganization of cancer work in hospitals. In Sydney efficient co-operation between research workers and those engaged in clinical treatment had not yet been placed on a satisfactory footing. A complete checking up of the radium issued by the Commonwealth was now in progress, and Dr. Holmes remarked that there had thus been brought to light cases of loss of radium and of insufficient protection of workers. Seven hospitals in Victoria were now receiving radon; more than 17,000 millicuries had been issued during 1931. The University of Sydney had made available for hire at a low cost by general practitioners 500 mg. of radium in 114 containers. Difficulties, it was added, were being widely experienced in consequence of the large number of patients who were applying for treatment, and of the continuing financial depression.

Classification and Recording of Cases

Work in the various consultative clinics was stated to be proceeding well, the cases being classified broadly as dermatological, gynaecological, and general surgical. It began to appear likely that special days would have to be set apart for the large group of breast cases. In Sydney the many patients with oro-pharyngeal, laryngeal, oesophageal, and rectal cancer who applied too late for treatment to be of any avail were giving great concern to the committees of management of these clinics.

The case-record system, adopted by the previous conference in 1931, has not proved as satisfactory in practice as was anticipated, and amendments are now being tried. One classification of cancer cases into four groups—operable, borderline, inoperable, and very advanced—while constituting an attempt to arrange the results of treatment according to the stage of disease, has not altogether succeeded, owing partly to differences of interpretation of these terms at various centres. Dr. Holmes invited the conference to consider whether such a classification might be so arranged as to vary in the case of different cancer regions. The compilation and forwarding of statistical summaries had also been unsatisfactory, in some instances because of the absence of some institutions of any adequate follow-up system. Progress in the control of cancer was being seriously retarded by such inadequacies. Dr. Holmes mentioned that in respect of cases treated by other means than radium very little information was available about the results obtained. This applied particularly to the sequels of surgical treatment and of *x*-ray therapy. He urged the importance of treatment centres publishing statistics of the treatment given and the results obtained; the follow-up system should be applied with equal care to all cases of cancer, irrespective of the method of treatment used.

Statistical Conclusions

Dr. Holmes announced that such records as had been received indicated that the increase in cancer mortality in Australia was mainly in the carcinoma group; in the case of epithelioma the death-rate curve, which had been rising since 1918, appeared now to have turned, while the sarcoma mortality rate remained fairly stationary. Diminution in this rate had occurred in cancer of the tongue in males, while that due to cancer of the female genital organs, though rising steadily, was not moving so fast as that for cancer of the other regions in the female, especially mammary carcinoma. In rectal and anal cancer the death rate per 100,000 mean population had more than doubled in the case of males in the last twenty years; it showed a corresponding but much less marked rise in females. The rate in males in respect of cancer of the digestive tract had also more than doubled in the past twenty years, and over 50 per cent of all male deaths from cancer were now attributable to involvement of the digestive tract.

Decisions of the Conference

A classification based on pathological considerations, and eliminating the rather vague terms "cancer," "malignant tumour," and "neoplasm" was considered. A small committee was appointed to review the whole question of the pathological and statistical classification of cancer, with instructions to consider of primary importance the provision and distribution of reliable and practical advice to medical practitioners on classification and the site of cancer with special regard to certification. The conference requested the Commonwealth Department of Health to draw the attention of the governing bodies of hospitals which possessed modern clinics to the importance of regular exchange at quarterly intervals of the nursing staffs attached to these clinics. A committee was appointed to consider increasing the screenage of radium and radon containers. Certain principles and standards of *x*-ray therapy were recommended for clinics. The Commonwealth Department of Health was asked to inaugurate a co-ordinated educational campaign throughout Australia.

Many of the clinical papers read at this conference are being published in the *Medical Journal of Australia*.

INCOME TAX

ASSESSMENT OF PROFESSIONAL INCOME ON CASH BASIS

[From Our Correspondent]

The judgements given in the case quoted may throw some light on the proper line of approach to the vexed question of payment of tax on fees received after sale of a practice.

A case, quoted as The Commissioners of Inland Revenue *v.* William Morrison, which was recently decided in the Scottish Court of Session, is of interest because it deals indirectly with a point which often arises in connexion with the assessment of medical earnings, but which rarely gets beyond the consideration of the original hearing before the Income Tax Commissioners. Briefly, the facts in the case were as follows:

Mr. Morrison was a professional engineer who had been assessed for some years on the "earnings basis." He desired to change over to the "cash basis," and the assessing authorities agreed. Subsequently, however, a dispute arose over the computation of the liability for the first year of the change. Mr. Morrison contended that the fees received for previous years, which had already figured in the former "earnings basis" calculations, should be excluded in arriving at the "cash basis" profit to avoid double taxation, and the Revenue contended that the "cash basis," if adopted, must be applied to all cash receipts of the year, whether previously reckoned as earnings or not. The four judges unanimously upheld the Revenue, and some of the dicta are of interest as having relevance to circumstances of much more frequent occurrence than the special facts of the particular case.

In the first place the Lord President referred to both methods of computation as allowable, and commented on the fact that the "cash basis" had "the merit of avoiding all the trouble which the second [the "earnings basis"] imposes on the taxpayer of calculating the 'outstandings' on current jobs." Inspectors of taxes seem to be somewhat less willing to concede the convenience of the "cash basis" than they used to be, and this judicial comment is, therefore, not without value to the practitioner. More than one of their lordships laid emphasis on the fact that it is apt to be misleading to regard tax as being paid on individual items brought into the credit of the income tax calculation. As Lord Sands said: "A tax is not paid upon individual items in the case of a business account of profits and gains; it is paid upon the profits and gains of the year, and the £1,362 was simply used as a factor in ascertaining the profits and gains of a previous year."

This principle applies to circumstances which not infrequently give rise to discussion—namely, the sale of the whole or part of a practice, without the book debts, which has been assessed to income tax on the cash basis. In such a case, say, of the sale of a practice by A to B as from March 31st, 1932, it may seem, at first sight, reasonable that A should continue to account for tax on his further cash receipts and B for tax on his cash income. Whether reasonable or not, it is clearly wrong in law. A accounted for tax on the profits and gains of the year 1931–2, and ceased to be entitled to the income of the practice after March 31st, 1932, and he is not assessable for any of the subsequent profits or gains of the practice. He will, doubtless, receive further payments, but these will relate back to other years for which he has accounted for his liability as computed from other "factors." The converse, of course, applies to B. He is legally liable to pay tax on the full profits and gains of the year 1932–3, whether computed on the "earnings basis" or on other "factors"—for example, on the "cash basis," as applied to the full earnings of the practice—in which case the cash recovered by A will have to be brought in as a factor relevant to the computation of B's liability as proprietor of the practice. Of course, if A and B decide, as a matter of mutual arrangement, to come to some compromise differing from their respective legal liabilities, there is no valid reason why they should not do so, but the Revenue authorities will normally insist on following the legal course, and the judgements in

Mr. Morrison's case support that view by laying emphasis on the fact that assessments are calculated on certain data, but are in respect of the income of the year for which they are made.

The Lord President's statement as to the mode of applying the "earnings basis" is worth putting on record. He said that

"according to the 'earnings basis' mode the actual cash receipts during the year and the actual cash outlays during the year are treated in the same way as before [that is, as for the "cash basis"]; but to the favourable balance thus brought out there is added the amount of the fees earned but not yet collected at the end of the year, and then there is deducted the amount of the fees earned but not yet collected at the beginning of the year."

In dealing with medical fees there is one important qualification to be added to this statement—namely, that when calculating the amount of the fees outstanding at the beginning and end of the year respectively the taxpayer is entitled to value each unpaid fee and deduct from the totals the aggregate of the sums which he anticipates losing by allowances and bad debts.

THE VOLUNTARY HOSPITALS IN A "SLUMP" YEAR

It is disappointing to receive in the midsummer of 1932 the *Hospitals Year Book*[1] and to find that its statistics relate, not to 1931, but to 1930. The year's returns for a thousand voluntary hospitals in Great Britain and Ireland are slow in accumulating, for the speed of a squadron is that of its slowest ship. Nevertheless, the experience of 1930 is useful, because that was the first year throughout which the effects of the world slump, beginning in 1929, were felt. It is remarkable how steady the hospital situation was in 1930, despite the heavy fall in the volume of trade, the rising taxation and Government expenditure, and the obstinacy of the unemployment figures. Hospitals and charitable institutions generally might be expected to meet the first blasts of the blizzard, yet the fact has to be recorded that in 1930 as compared with 1929 the total income of hospitals increased, and though the expenditure increased also the net surplus of income fell by only 6 per cent. In 1930 the hospitals received, for capital and maintenance, £15,612,750, and spent £14,870,402, leaving a surplus of £742,348. More than half the surplus, however, belongs to Scotland, where 82 per cent. of the hospitals had credit balances on their maintenance accounts, while in London this was true of only 51 per cent., and in the provinces of 74 per cent. Eight of the London medical school group of hospitals showed deficits, and four surpluses, while among the medical school hospitals in the provinces deficits and surpluses were almost equally divided.

It is interesting to note the sources from which hospitals receive their income. The figures in the *Year Book* are given in percentages, but it may be more instructive to show them in a different way. Every £ which the hospitals receive in maintenance income is derived as follows:

	Voluntary Gifts	Patients' Contributions	Public Services	Interest on Investments	Extraordinary Income and Other Receipts
	s. d.	s. d.	s. d.	s. d.	s. d.
London ...	7 7	5 4	1 4	3 4	2 5
Provinces	10 5	3 3	1 8	2 7	2 1
Scotland	7 11	1 4	10	4 1	5 9
Ireland ...	4 3	4 9	2 3	2 1	6 8

Voluntary gifts account for more than half the income of provincial, and for little more than one-fifth of that of Irish hospitals. Scotland finances her hospitals to the extent of 20 per cent. from endowments; public authorities provide 11 per cent. of the income of the Irish, and only 4 per cent. of the income of the Scottish hospitals. Extraordinary income consists in the main of free legacies, with, in Ireland, proceeds from sweepstakes. It should be made clear that "voluntary gifts" include workmen's contributions, Hospital Saturday Funds, and contributory schemes. The question is whether the last-named are affecting benevolent gifts. The figures for London have not been dissected in the *Year Book*, but for provincial hospitals, in 1930, voluntary gifts amounted to £1,665,841, and contributions, under schemes or otherwise, to £1,804,352. Both figures exceed the corresponding figures for the previous year. As to the expenditure of hospitals, between 80 and 85 per cent. of the maintenance costs are accounted for by provisions, surgery and dispensary, domestic, and salaries and wages. Taking the hospitals of Great Britain, out of every £ spent on these items, 4s. 5d. goes on provisions, 3s. on surgery and dispensary, 4s. 2d. on domestic expenses, and 8s. 5d. on salaries and wages.

Some impressive figures showing the work done during the year must be added:

	No. of Hospitals	No. of Beds	No. of New In-patients	No. of New Out-patients
London	148	16,012	249,442	1,825,804
Provinces	674	45,901	701,687	2,763,260
Scotland	99	8,843	150,089	539,244
Ireland	45	3,769	51,732	383,096

In 749 hospitals just upon 800,000 surgical operations under a general anaesthetic were carried out (this figure excludes London, the statistics for which are not available). But the best sign of the vitality of "voluntaryism" is the new buildings and extensions. During the last two years these include seven separate undertakings which have cost more than £100,000 each, nine which have cost more than £50,000, thirty-two which have cost more than £20,000, and thirty-one which have cost more than £10,000. In all, more than 300 voluntary hospitals have been adding to their accommodation or improving in one way or another their departments or equipment. The voluntary hospitals are, in fact, following Mr. Britling's example.

[1] *The Hospitals Year Book, 1932.* London: Central Bureau of Hospital Information.

ROYAL MEDICAL BENEVOLENT FUND

At the July meeting the committee voted fifty-seven grants amounting to £1,116 8s. 4d., as compared with £689 10s. voted at the July meeting, 1931.

Subscriptions and donations received during the month of July, 1932, were considerably less than the sum received in July, 1931. Contributions are therefore very urgently needed in order that the activities of the Fund may be maintained. Cheques should be made payable to the Honorary Treasurer, Royal Medical Benevolent Fund, 11, Chandos Street, London, W.1.

The following are particulars of a few cases helped:

M.B., C.M., aged 68. Only able to do very light work owing to ill-health. His relations give what help they can, but his total income is only £68 per annum. One supporter of the case wrote, "The circumstances are deplorable." Fund voted £40 in four instalments for twelve months.

L.F.P.S., L.R.C.P., aged 79. This applicant has been an invalid for four years with very severe cardiac trouble, and has not been able to work. He is entirely dependent on his niece, aged 42, who is trying to make a living by taking in paying guests. Fund voted £40 in four instalments for twelve months.

Daughter, aged 62, of M.R.C.S., L.R.C.P., is suffering from mitral disease, which renders her unfit for her work of nursing. The applicant has for some years been helped by an allowance of £6 a month from her married sister, but owing to business failure this help has now ceased. Fund voted £26 in four instalments for twelve months.

The Ladies' Guild of the Royal Medical Benevolent Fund still receives many applications for clothing, especially for coats and skirts for ladies and girls holding secretarial posts, and suits for working boys. The Guild appeals for second-hand clothes and household articles. The gifts should be sent to the Secretary of the Guild, Tavistock House (North), Tavistock Square, W.C.1.

British Medical Journal

SATURDAY, AUGUST 27th, 1932

MENTAL TREATMENT ACT: THE FIRST YEAR

The annual report of the Board of Control, for the year 1931, Part I,[1] which was issued a few days ago, has on this occasion a greatly enhanced interest, in that it includes an account of the working of the Mental Treatment Act during its first year. The ultimate aim of the framers of the Act, which came into operation on January 1st of last year, was clear. In brief, it was to promote the homologation of the treatment of mental and bodily ailments, or, in other words, to extend and strengthen the co-ordination of psychiatry and general medicine in every department—in the laboratory, the clinic or out-patient department, and the hospital alike—and, by statute, to open freely to the sufferers from mental disorder (subject only to necessary safeguards) the most appropriate means of treatment at the earliest possible moment. But, as we wrote last year (*British Medical Journal*, 1931, ii, 151) when dealing with this subject, compromise between separate and sometimes opposing interests—those of the patient and those of the community—was inevitable, and, as happens to most compromises, a certain amount of dissatisfaction was expressed when the Act was promulgated. In particular, criticism has been directed against the conditions governing the admission and continued treatment of temporary patients—that is, patients incapable of volition and likely to benefit by temporary treatment without certification—some maintaining that these conditions were destructively tight and others that they were dangerously loose.

Leaving this matter to its due place in this notice of the year's results, it will be recalled that under the first section of the Act any person who wishes to submit himself to treatment for mental illness may be admitted as a "voluntary patient" into a public mental hospital, or into a hospital, nursing home, or place approved by the Board of Control, without certification or reception order. For many years "voluntary boarders," as they were formerly termed, could be received into registered hospitals and licensed houses for private patients, but with the two exceptions of the City of London Mental Hospital and the Maudsley Hospital the doors of the public mental hospitals of England and Wales were closed to all but the certified insane until the Mental Treatment Act came into being. It is perhaps not too much to say that had this section been the sole achievement of the Act a considerable step forward would have been taken. The actual numerical results of this section are interesting. Of the total direct admissions (24,212) to all forms of care, 14 per cent. were received as voluntary patients, but of the total direct admissions (20,945) into county and borough mental hospitals only 7 per cent. were so received.

Financial considerations have no doubt had a severely restricting effect. Mindful of the fact that most, though by no means all, of the patients likely to be admitted on a voluntary footing would be early and non-certifiable cases, it was widely felt by the governing bodies of county and borough mental hospitals that special provision should be made at all public institutions which were not already in the fortunate position of having suitable accommodation for this class of patient. From this point of view the Mental Treatment Act could hardly have been launched at a less favourable time. The financial crisis, which enforced a slowing down of all health services, falling on top of an acute shortage of accommodation in many of these institutions, caused some local authorities, the Board says, to place too rigid a limit on the admission of patients under this section, or even, as in the whole area covered by the Lancashire Mental Hospitals Board, to exclude them altogether. Yet, notwithstanding that over some large areas either no, or few, voluntary patients were admitted during the year, the fact that at some hospitals—notably Wakefield, East Sussex, Leicester City, Portsmouth, Ipswich, the North Riding, and Cardiff—the proportion of voluntary patients ranged from 20 to as much as 33 per cent. of all direct admissions leaves no room for doubt that the future will increasingly demonstrate the value of this important legal dispensation. The experience of the registered hospitals and licensed houses for private patients where this provision has been long established, and in which the proportion of patients voluntarily seeking admission and received without certification has risen during the last twenty years from 19 per cent. to 65 per cent. and 50 per cent., itself suggests that only time and added acquaintance with the working of a new enactment are required to secure equal and orderly expansion of the voluntary system in public institutions. A striking feature revealed by the report is the wide difference between area and area in its application. Thus, of those hospitals which began receiving voluntary patients twenty-seven did so to less than 5 per cent. of their direct admissions; twenty to the extent of from 5 to 9 per cent; fifteen to the extent of from 10 to 14 per cent.; and seven from 15 to 19 per cent.; the high proportion in seven more has already been mentioned.

The same irregularity is to be observed in the employment of temporary treatment. Only 2 per cent. of the total direct admissions into all forms of care were admitted as temporary patients during the year. This result the Board describes as disappointingly small, as indeed it is. During 1931 only one voluntary general

[1] Eighteenth Annual Report of the Board of Control, for the Year 1931. Part I. London: H.M. Stationery Office. 1932. (2s. net.)

hospital and eight nursing homes were approved for its use, and into these establishments of forty-five patients ten were of temporary status. Of the forty-five licensed houses approved for temporary patients 9 per cent. of the total direct admissions (1,205) were of this class, and in the registered hospitals the proportion was 6 per cent. of their 940 direct admissions. At no fewer than forty-three of the ninety-eight county and borough mental hospitals, including some of the largest in the country, no temporary patient was admitted. On the other hand, whilst temporary patients were in general admitted in small numbers, at five mental hospitals the proportion of temporary patients ranged from 10 per cent. of the direct admissions (Ipswich and the City of London) and 11 per cent. (Hereford and Scalebor Park) to no less than 26 per cent. (Derby Borough).

Money, time, and experience are probably as necessary for the development of temporary treatment as for the voluntary system, though perhaps for the former the order of these three desiderata should be reversed. "It is impossible," the report states, "to visit any mental hospital without finding non-volitional cases sent in under certificate, although by the use of the new provision certification, with its attendant disabilities, this might easily have been avoided." This somewhat unfortunate position, the Board says, may be to some extent due to a lack of acquaintance on the part of general practitioners with the possibilities which the new Act offers of treating these cases without certification. It is also possible that public assistance officers have not always been adequately instructed on this point. The Board fears that in some areas the trifling cost of a second certificate may have been allowed, out of a misguided zeal for economy, to deprive the rate-aided patient of the benefit Parliament meant to give him. "It would, indeed," it says, "be unfortunate if the necessity for a second recommendation, which Parliament inserted as a safeguard against the risk of improper detention, should have the effect of limiting the privilege of treatment on a temporary basis to the well-to-do classes." We are glad to note that the Board proposes to take up the latter possibilities with the local authorities.

With regard to the first suggestion, however, it is probable that in many areas outside centres of large populations the general practitioner has had all too little opportunity of becoming practically acquainted with the special and technical aspects of mental disorders, and the possibilities of treatment and disposal of patients under the new dispensation, and that this may to some extent explain the apparent indifference to the provisions of Section 5 of the Act in so many areas. In this connexion the following words in the report may have some significance: "But in the areas *in which the Act has been energetically worked* [our italics] the number of voluntary and temporary patients admitted has been substantial, and in one area the patients in these two classes amounted to nearly 45 per cent." Noteworthy and encouraging progress has been made with the establishment of out-patient clinics in recent years, so much so that a regular network of clinics has been organized in some of the county areas. Although we are unaware of what the words "areas in which the Act has been energetically worked" may imply, it may be safely assumed that these areas will coincide with those where out-patient clinics have been established at general hospitals or elsewhere in association with the mental hospitals in the area, and where, by means of the clinic or otherwise, the medical staff of the mental hospitals are in close and frequent touch with their medical brethren in the area. It can hardly be accidental, for example, that Wakefield was the first public mental hospital to open an out-patient department, and is now among those institutions which head the list in working the new Act.

Temporary treatment without certification is so novel a procedure that the Board has considered it hardly profitable to supply much in the way of statistics. At this stage, indeed, comparative deductions might be misleading, but from the figures given in the report one positive result has been obtained. About one-quarter of the total number of patients (659) directly admitted into all forms of care during the year (the majority, in the very nature of things, gravely ill, being incapable of expressing themselves as willing or unwilling to receive such treatment) either recovered or were discharged relieved without certification. Disappointing as the numerical results of this section of the Act during the last year may be, the high proportions dealt with under this provision at a few hospitals shows conclusively that the explanation of its exiguous employment in so many areas is to be sought neither in the words of the Act nor in their official interpretation, but in local and happily removable impediments.

So much attention has been focused on Section 5 that there is some risk of overlooking less striking but equally essential provisions, such as the power given to local authorities to provide out-patient clinics, to make provision for after-care, and to undertake research in relation to mental illness. Reference has already been made to the vital place out-patient clinics occupy as a link between the specialist services of public mental hospitals and the community at large through their private practitioners, and it is gratifying to learn that clinics have already been established at sixty-one general hospitals, nineteen mental hospitals, and eighteen other premises. Those of our readers who have studied the Annual Report of Council, 1931–2, will be familiar with the Association's views as to the position of the general practitioner in the treatment of mental disorder, and his relation to these clinics. That report opened by pointing out that the treatment of patients suffering from mental illness is becoming of increasing importance to the private practitioner in his daily work. It is equally true that the co-operation of the private practitioner is becoming of increasing importance not only to the working of the Mental

Treatment Act but to the recognition and treatment of mental disorders in their beginnings.

(Further commentary on the report appears at page 416.)

THE FUTURE OF THERAPEUTICS

A centenary meeting is the natural occasion for a general review of past progress and of future prospects, and Professor J. A. Gunn, in his recent address to the Section of Pharmacology and Therapeutics (printed at page 389 this week), has raised questions which deserve the careful consideration of the medical profession. The first question is whether the advances made in therapeutics have been commensurate with those made in other branches of medical science, and a second question, of even greater importance, is whether our present methods are likely to yield an adequate harvest in the future. During the last half-century we have witnessed a number of remarkable advances in curative medicine, notably the discovery of the antitoxins, endocrines, and vitamins, and the development of chemotherapy. Nevertheless these remedies are applicable to only a small proportion of human disease, and it must be confessed that but little progress has been made in the treatment of the common ailments that afflict the majority of patients who enter the medical departments of a hospital. On the other hand, if we consider surgery, preventive medicine, or pathology, we find that these sciences in their present form are entirely a creation of the last century. There is in particular a remarkable contrast between the relative rates of advance in methods of diagnosis and in methods of treatment. If one of the founders of the British Medical Association could visit a modern hospital one of the changes that would impress him most would be the extraordinary development of methods for the diagnosis of disease. His surprise at these marvels would be great, but perhaps not greater than would be his surprise on learning that in a large proportion of cases the culminating result of all this elaborate technique was the application to the patient of curative methods which not only were perfectly familiar, but whose value he knew to be dubious.

A general survey of the forward movement of medical science during the past hundred years suggests that therapeutics as a whole has lagged behind the other main branches of medicine, even when allowance is made for the isolated fields in which striking progress has been achieved. This failure to advance cannot be attributed to any high level of efficiency hitherto attained, and the reason propounded by Professor Gunn seems to be the true one—"simply neglect of, and some lack of interest in, therapeutics." As Professor Gunn points out, this state of affairs is to some extent inevitable, because rational therapeutics cannot develop until methods of accurate diagnosis have been established. Unfortunately the development of accurate diagnosis does not necessarily cause the development of rational therapeutics, and therefore we have no guarantee that the future will prove more satisfactory than the past unless steps are taken to encourage interest in therapeutic research. The problem is of particular interest to the medical profession in this country because we have taken less than our fair share in such advances as have been made in recent years. We accept as a matter of course the fact that Germany supplies nearly all the new synthetic remedies, and although our schools of physiology are strong most of the successful applications of physiological discoveries to clinical medicine have come from America. This is not a mere accident; it arises from the circumstance that we have less provision than have Germany and the United States for organized study and research in therapeutics, while the general trend of development makes advance in this subject more and more dependent on such team work.

Discovery and invention are incalculable things, and the lone genius sometimes succeeds where organizations fail; but consistent progress in a science can only be achieved if it attracts enough recruits of the right calibre. Moreover, the literature of sciences in general increases by geometrical progression, and their technique is becoming more and more complex and difficult to acquire. Both these factors increase the difficulties of part-time workers in science and make it more essential to have an adequate number of full-time workers. In the case of therapeutics, moreover, team work is almost essential, and this implies organization. For the discovery of a new remedy the collaboration of organic chemists, pharmacologists, and clinicians is needed, and provision must be made for a large amount of routine work. The investigation of the possible therapeutic properties of new compounds involves testing dozens of drugs upon animals before one is found that is worth a clinical trial, and with the selected drugs there will probably be many "misses" before a single "bull" is registered. Professor Gunn has outlined the kind of organization that is required to carry through work of this nature. It is important to emphasize the fact that no such organization exists in this country, that at present we have not the necessary personnel, and that the position is likely to be worse rather than better in the future, because there is little encouragement for young men of brains to contemplate a career as whole-time research workers in pharmacology or experimental therapeutics.

The question before the country is whether it is worth while to organize research in therapeutics on an adequate scale. The results of research are of course wholly unpredictable, and disappointments are far more frequent than successes, but for practical purposes we should assume that most of the discoveries in therapeutics that can be attained by lucky chance have already been made, and that in the future success will come chiefly as the result of organized hard work. It is therefore no use expecting to get the results without providing an adequate organization for this purpose.

BRITISH ASSOCIATION IN YORK

Each year it becomes more difficult and more invidious to select from the transactions of the British Association for the Advancement of Science a list of papers that may be justly held to have a direct interest to the medical profession. Unremittingly the pure and applied sciences are encroaching upon medicine as an art ; and medicine itself, as its scope extends, makes ever-increasing demands upon specialized fields of scientific inquiry. It is interesting to recall, as Sir E. Sharpey-Schafer mentioned to the Section of History of Medicine at the recent Centenary Meeting (August 20th, p. 375), that as late as the middle of the nineteenth century anatomy was regarded as the only essential foundation to the study of medicine ; and, by contrast, to consider the present state of affairs as revealed in the programme for the forthcoming meeting of the British Association (which will be held in York from August 31st to September 7th). Material of profound interest to the medical profession is to be placed before practically every Section—certainly those of chemistry, zoology, engineering, anthropology, psychology, botany, and educational science. The Section that normally would contribute the bulk of the papers with a bearing on medicine—namely, that of physiology—is not to be represented at York in view of the fourteenth International Physiological Congress at Rome. In the Section of Chemistry Professor G. C. Bourne will open a discussion on water pollution, at which papers will be read on the decomposition of sewage in river water and the effects of pollution on the biology of the non-tidal reaches of the Tees. The Section of Zoology, before which Lord Rothschild, F.R.S., will deliver a presidential address on the pioneer work of the systematist, will discuss, among other subjects, iodine compounds and the level of activity of animal tissues ; the influence of the processes of feeding and digestion upon evolution ; the mechanism of animal movements ; and the origin of body fluids. In this Section, too, Professor R. T. Leiper will contribute the opening paper to a symposium on helminthology, taking as his subject the applications of helminthology to medicine ; and other speakers will treat of the subject in relation to veterinary medicine, the biological control of pests, and the work of the Bureau of Agricultural Parasitology. In the Section of Psychology practically every paper has some medical interest. Among the subjects to be discussed are: the relation of the classification of the colour-blind to the tests for colour-blindness ; individual differences in colour discrimination ; variations of colour memory with wave-length; suggestion, hypnotism, and the will; Gestalt psychology in relation to other modern psychological systems ; temperamental differences in the behaviour disorders of children ; the relation between educational backwardness and behaviour difficulties ; the value of vocational guidance ; and the bases of intelligent and instinctive behaviour. To this Section Professor W. McDougall, F.R.S., is reading a report on a Lamarckian experiment designed to test whether increased facility in a stock of rats trained to a specific task could be due to a "social" transmission or favourable selection. The programme of the Engineering Section includes a paper on the suppression of noise ; and of the Anthropological Section on the differentiation of human race groups on the basis of serological tests. These are a very few and perhaps arbitrary selections from a comprehensive programme. It would be difficult, indeed, to find in any of the Sections papers from which some medical practitioners, at any rate, would fail to extract material of concern to them in their professional work. The published programme could serve as a pretty accurate blue print of the advance of British science in the past year.

PREVENTIVE MEDICINE IN GENERAL PRACTICE

In the *Journal of the American Medical Association* for June 11th last appear three articles, together constituting a symposium which might be well described under any of their titles. These are: "Organized medicine and public health," by Dr. Baker of Montgomery, Alabama ; "Present-day trends of private practice," by Dr. Fishbein of Chicago ; and "Preventive medicine in general practice," by Dr. Lee of Boston. It is interesting to study them in connexion with the paper which Sir George Newman read as President of the Section of Public Health at the recent Centenary Meeting, and which was published and commented on in the *Journal* of July 30th (pp. 190 and 209). They show that in America, as in this country, it is being recognized more and more that the private medical practitioner, and especially the general practitioner, is one of the most powerful agents of preventive medicine, and that he may claim to rank at least equally in this field with his two great colleagues—the public health medical officer and the research worker. It is a mistake to try to gauge the relative importance of the work of each of these three: still less is it necessary for any one of them to vaunt himself above the others. They should be regarded as a team, each of whom must avail himself as fully as possible of the services of the others in order that full public advantage may be secured. In this country, as perhaps everywhere, the discoveries of the research worker take far too long before they are actually put into common practice ; the public health medical officer too commonly still regards the private practitioners of his area as engaged in a separate sphere of professional work ; and those private practitioners continue to pursue their daily activities in preventive as well as curative medicine without realizing, as they should, that they ought to be a continuous and integral part of the public health organization of the area. Private practitioners were the earliest agency in the prevention of disease. They have never ceased to be such agents. Yet it is only now that they are beginning consciously to recognize themselves—or that the public is beginning to recognize them—as one of the most effective and essential of such agencies. The articles to which we draw attention demonstrate that this preventive work of the general practitioner will be one of the main developments of the immediate future. It is one of the highest types of service he can render, not merely to his patient, but to society. As Dr. Baker puts it: "Public health activities are sometimes mistakenly conceived to be inconsistent with the best interests of organized medicine. A careful examination of the facts will reveal that the highest type of State-supported preventive medicine may be conducted with full and complete regard for the prerogatives of private physicians as well as for the rights of the general public."

"THE MEDICAL CRISIS"

In the second number of the *Quarterly Bulletin of the Health Organization of the League of Nations* (English edition), is an important article on "Medical education in Germany." The whole of this contribution is valuable as setting out clearly and shortly the methods of medical education in the German Reich and in its several Federal States. They differ materially from the methods followed in this country, though certain reforms now being discussed, or already sanctioned, will tend to bring the German system of training and examination a little nearer to British lines. The article is prefaced by an introductory section, which states in a somewhat alarming fashion the present position of the medical profession in Germany. Its first sentence is, "The medical crisis has, in Germany as in other civilized countries, assumed very serious proportions." The fundamental cause of the situation is said to be the tremendous growth of scientific research and knowledge during relatively recent years. This has resulted, in the medical as in other fields, in extreme specialization, with consequent dispersion and isolation of effort, absence of synthesis, and "studying and treating sickness from too one-sided a point of view while neglecting the patient himself." A swarm of specialists is ousting the family doctor, and a large number of his patients are being removed from his observation and treatment, since, following the same tendency towards specialization, the graver cases usually go to hospitals and many of the less severe to clinics. A mechanization of diagnosis and treatment, mainly in institutions, is being evolved, and this tends inevitably to dehumanize medicine. The German health insurance system, with less freedom of choice than here, and greater stress on institutional treatment, is described as acting in the same direction. The result of all this is that there is a diminished public confidence in the medical profession. This, together with the great increase in the number of doctors of late years and the turning towards mysticism and the supernatural which has gained so much since the war, and which the quack is better able to cope with than those who are scientifically trained, has brought about a very severe economic crisis in the profession. "There is considerable distress among elderly doctors and a great deal among the young ones, who have the utmost difficulty in building up their practices." The picture strikes one as slightly exaggerated, but it is painted by those who are in a position to know the truth. It is worth contemplating seriously, for many of its main features are those which in England would appear in miniature. The remedies suggested are a tightening up of educational requirements, an increase in the disciplinary and advisory powers of both official and voluntary medical associations or bodies, with perhaps a closer restriction of the "authorization to practice," and the prohibition of unqualified practice altogether. The various reports of the Association Professionnelle Internationale des Médecins in its *Revue Internationale* have shown us that the position of the medical profession in this country is in most respects better and more secure than it is in any other; but there can be no doubt that the economic stress on the profession here is just now very great, and a warning of possible developments does not come amiss.

THE EDUCATIONAL NUMBER, 1932

Our next issue, dated September 3rd, will be the annual Educational Number of the *British Medical Journal*. Its contents, as in previous years, will include a full account of the requirements of the General Medical Council and of the universities and other licensing bodies in Great Britain and Ireland, as well as information about the opportunities offered by the various medical schools and other teaching institutions, and the fees charged by each. The details given have been revised and brought up to date by the authorities concerned. These sections, the object of which is to furnish a handy guide to intending students of medicine, are supplemented by articles intended for newly qualified practitioners on such matters as post-graduation study in Great Britain, the public medical services, tropical medicine, psychological medicine, and the various special diplomas. In the sections dealing with the public services will be found a concise account of the present terms and conditions of service in the R.N.M.S., the R.A.M.C., the I.M.S., and the R.A.F.M.S. The opening articles for this year's Educational Number are Mr. H. S. Souttar's address entitled "The Future of Medical Education," and a paper by Dr. H. Crichton-Miller on "Primitive Man and the Modern Patient."

DR. COX'S TESTIMONIAL FUND

PRESENTATION BOOK

For the benefit of subscribers and others who have been unable to see the Presentation Book given to Dr. Alfred Cox by members of the British Medical Association at the Centenary Meeting on July 23rd, Dr. E. Rowland Fothergill, honorary secretary of the General Committee, sends, on behalf of the Executive Committee, the following detailed account of the book, prepared by Messrs. Raphael Tuck and Sons, who have carried out the work.

The book is bound in royal blue leather with an inscription in gold. It contains the names of approximately seven thousand people who have contributed to the Dr. Cox Testimonial Fund, the lists of the Executive and General Committees appearing on decorated pages at the beginning.

The inscription on the cover, in gold, runs:

TO
ALFRED COX
O.B.E., M.A., LL.D., B.S.

The inscription on the first page inside is as follows:

> "The names written on the following pages are those of the subscribers to the Alfred Cox Testimonial Fund. The Testimonial includes a Portrait of Dr. Cox, painted by Sir Arthur Cope, R.A., and presented to the British Medical Association, and this book together with a cheque given to Dr. Cox personally on the occasion of his retirement from the office of Medical Secretary of the Association after twenty-five years of distinguished and devoted service. The subscribers make the presentation as an expression to Dr. Cox of the appreciation, gratitude, affection, and goodwill of his fellow members and personal friends alike at home and beyond the seas. July, 1932."

The book is in five sections—England, Ireland, Scotland, Wales, and Over-seas—each section being marked by a coat of arms. In the Oversea section five coats of arms represent Australia, Canada, India, New Zealand, and South Africa, and are united by five scrolls surrounding a miniature galleon. The names and addresses of subscribers appear under the several subheadings of the Divisions of the British Medical Association in which they reside. Each name and address is written in manuscript on fine paper, with appropriate illuminations in gold and colours.

HEALTH OF LONDON SCHOOL CHILDREN

REPORT FOR 1931

The report of the L.C.C. School Medical Officer for the year 1931[1] is one of steady progress rather than of any spectacular developments.

RESULTS OF INSPECTION

The number of elementary school children examined in the three groups—entrants, aged 8, and aged 12—was 180,245, and another 38,754 were examined in the term before they left school. The school doctors see each year considerably more than half of the children attending school, and a refusal to submit the child to examination is extremely rare. Parents are encouraged to be present ; 89 per cent. of them attended the inspection of the entrants and 40 per cent. that of the leavers. Of the children referred for treatment, the majority needed dental care, the whole figure being 42.8 per cent. and the non-dental cases 18.9 per cent. The report last year noted that the proportion of poorly nourished children had reached a record low figure of 4.8 per cent., and the same figure appears this year. The cleanliness, like the nutrition, of London school children has improved enormously ; 95.2 per cent. were free from even traces of nits or lice in the hair, and only 0.3 per cent. showed any evidence of body vermin. These results are a great tribute to the devoted work of the school nurses. There is a continued improvement in the dental condition—namely, 1.5 per cent. since the previous year. Since 1924 there has been no diminution of serious dental decay among entrants, but in other groups the proportion has fallen almost to half, thus reflecting the efforts of school dentists and treatment centres. About the same number of children suffered from rickets, enlarged tonsils and adenoids, and running ears as in 1930, but there was continued improvement in vision, probably owing to lessened prejudice against wearing glasses. The leavers also showed a steady superiority over the 12-year old group in nutrition, in cleanliness, and in general health, the only exceptions being the dental condition and the incidence of spinal curvature.

At the end of 1931 the Council had seventy-three centres and seventeen hospitals in its medical and dental treatment scheme, and nearly 307,000 children were treated. The provision for *x*-ray treatment of ringworm has again been decreased owing to the gradual elimination of this condition. It was necessary to augment the number of beds available for tonsillectomy. Towards the end of the year, however, there was a considerable falling-off in the number of cases requiring treatment, which is not surprising, since more than one thousand school children in London have had their tonsils and adenoids operated on in the last decade. An interesting comparison has been made between the results at an ordinary dental clinic and those at the special centre at Hackney Wick, where particular stress is laid on prophylactic cleaning and polishing and use of the toothbrush. It was found that the Wick children undoubtedly showed a better dental condition ; the report hesitates to ascribe this to any one factor, but attaches some importance to the fact that the treatment was throughout conceived and executed on prophylactic and remedial lines.

RHEUMATISM

There is a reduction in the figures for heart defect, which may be ascribed to the greater care of rheumatic conditions. The Council's rheumatism scheme cared for over 10,000 children during the year, and four new supervisory centres and more beds were provided ; 943 children were nominated for residential treatment. As before, girls outnumbered boys. One thousand attacks of rheumatism distributed over a period of five years were studied in relation to monthly variations in rainfall, air, humidity, air and earth temperature, and hours of sunshine. Contrary to popular opinion, an increase in rheumatism was found when the rainfall was below normal. Increase in rheumatic incidence seems to depend on a combination of rainfall below normal, reduced sunlight, and low air temperature. A decrease in rheumatism, on the other hand, is produced by the association of rainfall above normal, more than the average amount of sunshine, and high air temperature. At the Hammersmith and Royal Waterloo Centres an investigation has been made into the sleeping conditions of the children ; of 455 only forty-four had a bed and the room to themselves, and the report emphasizes the impossibility of securing the necessary amount of rest when the bed or room is shared. On the whole, the diets of the children appeared to be deficient in protein.

HYGIENE

The reorganization of schools on the lines of the Hadow Report is progressing. Provision for education in the open air is increasing ; there are now nine non-tuberculous and six tuberculous open-air schools and five country and seaside convalescent camps, in addition to the 200 open-air classes in playgrounds and parks. Experience has shown that there are two types of weakly and anaemic children in the London schools. The bronchitic type thrives on open-air treatment, while the rheumatic type requires warmth and coddling. Hygiene and sports are now generally taught to the older children, and the best results are obtained where the teacher is to some extent a specialist. Nevertheless, the time devoted to this subject is still inadequate.

CHILD GUIDANCE, DELINQUENCY, AND MENTAL DEFECT

Parents have, as a rule, shown themselves most interested in the work of the child guidance clinic to which children are referred. In only a very few cases has it been found necessary to place the children away from home. The parents are always advised in a common-sense way, so that they can understand the reason for the treatment suggested ; they are then always willing to act on it. During the year sixty-three boys and forty-five girls were referred to the clinic at Canonbury and 339 to the Maudsley Hospital, while during the last four years the East London Child Guidance Clinic has seen 393 children. The majority were referred for backwardness, nervousness, and behaviour problems, but the Maudsley Hospital also had nineteen certifiably defective and nine psychotic children. Observations in the play-room have proved of great value, and the results of treatment are on the whole encouraging: a satisfactory result is obtained in about 60 per cent. and a fair result in about 20 per cent. more.

There are now just under 1,000 children who have left the special schools for mental defectives and are under supervision ; the majority of them are employed. There are seven residential special schools for the blind, deaf, and mentally defective, accommodating 355 residents and 216 day scholars, and three industrial schools with a total accommodation for 357. Each school has a medical officer and a dentist attached to it. The Ponton Road place of detention received 866 children during 1931, about half of them above school age. By far the commonest offence was stealing, which begins early in life and becomes increasingly prevalent in both

[1] London County Council. Annual Report of the Council, 1931. Vol. iii (Part II). Public Health (Report for the Year 1931 of the School Medical Officer). London: P. S. King and Son, Ltd. 1932. No. 2905. (1s. 6d.)

sexes as the years go on. Premeditation seems to play a small part in juvenile theft, and the cause seems to lie rather in the natural acquisitive instinct than in any deeper psychological reaction. The next commonest charge is that of being beyond parental control. The home conditions of these children are almost always bad, and the most refractory of them settle down and behave normally after a few days in the institution. The percentage of physical defects in these children is above the average. Each child admitted is given a full mental test, which reveals a marked disparity between the actual intelligence and the educational attainments of the delinquent, the latter being far below the former. Taking boys and girls together, 90 per cent. show more or less retardation on education tests, while 76.4 per cent. are of more or less blunted intelligence. Boys accused of stealing and associated offences show on the average 2.9 years' retardation, while those charged with sexual offences show five years' retardation, but the number of the latter is small. Only 5 per cent. of those admitted during the year were mentally defective.

Physically Defective Children

A careful study of the children suffering from heart disease has been made. On the whole, the teachers would be glad to see these children in special schools, as it is difficult to deal with them in a general class. Physically defective children seem to be less good at work requiring concentration or applied thought than at subjects which have emotional appeal, and to need more careful moral supervision at the adolescent stage. To leave a physically defective child in an ordinary class often means the development of a sense of inferiority and of being "different," which can only be overcome by a long and difficult period of intensive discipline when he gets to the special school. There appears, however, to be very little feeling of inferiority among heart cases and those whose affliction does not make them look abnormal. Unwise home treatment is one of the greatest difficulties, and it is of incalculable value for the child to find itself "one of a crowd." School absences are also avoided, as the child need not lose instruction for unreal or minor complaints, bad weather, or the fussiness of the parent. While children are away at the special school attempts are made by the care committee workers to improve home conditions and to educate parents.

During the year the council's aural surgeon saw 351 children suffering from various affections of hearing. There was no deafness due to cerebro-spinal meningitis. There were 218 children in schools for the blind. The percentage of cases of ophthalmia neonatorum remains practically unchanged (21), but the actual number of cases of blindness from the disease is diminishing. The percentage of congenital defects has increased, the increase being relative and mainly due to the great fall in the incidence of interstitial keratitis and allied conditions.

Infectious Diseases

The year 1931 showed a decrease in cases of diphtheria, scarlet fever, measles, mumps, and ringworm, but a slight increase in ophthalmia, scabies, and chicken-pox, and a considerable increase in whooping-cough. The decrease in small-pox was from 1,774 in 1930 to 604 in 1931. Diphtheria carriers continued to be treated at the London, St. Mary's, and Guy's Hospitals; when a positive swab is obtained the tonsils and adenoids are removed, but no satisfactory treatment has been found for the carrier with an atrophic nasal condition. The best method seems to be a daily saline douche combined with monthly iodoform gauze packs on three consecutive nights. St. Mary's Hospital has had success with autogenous vaccines, but Guy's Hospital is discontinuing its stock vaccine for lack of evidence that it is of any use. The percentage of children showing vaccination marks at their medical inspections is slightly less than last year, but the recent prevalence of small-pox seems to have led to a considerable amount of primary vaccination at school age. During the year fifteen boys and five girls were admitted to the post-encephalitis lethargica unit at Winchmore Hill.

A number of institutions under the care of the Council carry out active immunization against diphtheria, with excellent results: diphtheria is now practically unknown in these schools. The prophylactic used is formolinized toxin.

TREATMENT OF MENTAL DISORDER

Following the course adopted last year the annual report of the Board of Control for 1931, on which a leading article appears at page 411, opens with a reference to the Mental Treatment Act. It is the unfortunate but inevitable corollary of the occurrence of mental disorder that its treatment entails in very many cases the adoption of all sorts of legal formalities. Various enactments have come into being from time to time in accordance with the increasing realization of the need for better care and treatment of the individual and for greater security for the community. Sometimes the one consideration preponderated, sometimes the other. These respective and apparently conflicting considerations have never been so happily harmonized as in the Mental Treatment Act of 1930, whereby a successful compromise has been achieved between the patient's need of early treatment and the necessity for the safeguarding of his legal rights.

Voluntary Admissions

In virtue of the provisions of this Act, patients may present themselves voluntarily for treatment at a public mental hospital from which hitherto they were debarred unless certified to be insane. This has been an undoubted boon to many, imparting a sense of security to the patients themselves by the knowledge that they could seek treatment the moment the burden of their illness became too great to bear; and it has proved a stimulus to the hospitals, inasmuch as patients of this category are admitted at an earlier stage of their illness, where their presence in increasing numbers tends to create a more truly hospital-like atmosphere than that to which mental hospitals had in the past been accustomed. Voluntary patients presenting themselves either to public mental hospitals or to general hospitals are for the most part suffering from melancholia, but psychoneurotics of the severer types are not uncommon and even paraphrenics seek admission, partly because of a dim realization of the need for treatment but more in order to escape from their imagined persecutions. That the privilege so long afforded the well-to-do of securing treatment on a voluntary basis should have been so long denied to those who could not afford to pay the fees of a private establishment is a matter for astonishment, but though the wheels of the legal machinery of the land move slowly it must be admitted that the Mental Treatment Act has done more than rectify this anomaly.

More even than the melancholic sufferer, it was the puerperal delirious patient whose disposal was so great an anxiety to the family doctor. The excitement which invariably accompanies the toxic confusion, the dangers to which the child and the mother herself are exposed, the likelihood of the illness becoming a protracted one, and the impossibility of providing adequate nursing facilities at home—all these considerations pressed on the

[1] Eighteenth Annual Report of the Board of Control, for the year 1931. Part I. London: H.M. Stationery Office. 1932. (2s. net.)

doctor the necessity for instant admission of his patient to hospital. But before the Mental Treatment Act came into operation admission to hospital meant admission to a mental hospital, and this again meant certification, and in the case of the poorer classes their first acquaintance with the machinery of the Poor Law and all its attendant sense of degradation. In such cases now the practitioner no longer certifies. He "recommends." The distinction is not merely one of name. The intervention of the magistrate is not required: merely the considered written statement of two doctors—one the family doctor and the other a practitioner on the approved list of the Board of Control. They may examine the patient jointly or separately. The form for recommendation of a temporary patient requires it to be stated that the patient is non-volitional—that is, that he has no power of saying "yea" or "nay" in the matter of his admission; that he is likely to benefit by temporary treatment; and that his recovery may be expected within a period of six months.

TEMPORARY PATIENTS

Temporary cases constitute an entirely new category, both for private and for public hospitals. They are now also admitted to general hospitals as well as to mental hospitals of any variety. They need not, of course, conform to the type of the puerperal delirious case instanced above, but they must in fact be non-volitional. That is the important matter. That they should be deemed likely to benefit by temporary treatment and that recovery may be expected within a period of six months may, with very rare exceptions, be assumed.

With the thought of such cases in mind, cases of every-day experience in general practice, it is with the greatest interest that we turn to the latest report of the Board of Control to find out to what extent recourse has been had to these enlightened provisions of the Mental Treatment Act, and to gauge if possible the result of such provisions on the progress of these types of mental illness and the ultimate effect on our hospitals, both general and mental.

EFFECTS OF THE NEW ACT

It is heartening to find that, with regard to the admission of voluntary patients, the Act has been widely welcomed and in many cases energetically put into operation. Still, of the total direct admissions (20,945) into county and borough mental hospitals during 1931, only 7 per cent. were voluntary. The percentage of voluntary admissions into all forms of care—that is, to registered hospitals and licensed houses as well as to public mental hospitals—was 14; but since the two former have been in the habit of accepting such patients prior to the Mental Treatment Act, the lower figure affords a better indication of the popularity of this provision. Owing to the lack of accommodation, no voluntary patients have been admitted to any mental hospital under the control of the Lancashire Hospitals Board. Doubtless the exhortations of the Board of Control will have the effect of raising the percentage of voluntary admissions throughout the country, with corresponding benefit to patients and hospitals alike.

The Board laments the small number of admissions of patients of the "temporary" category. Of the total direct admissions to public mental hospitals only 2 per cent. were of the "temporary" status, and forty-three of such hospitals received no patients at all of this category. It is pointed out that many non-volitional cases are still being certified. Doubtless this is due mainly to the fact that many practitioners are not yet sufficiently acquainted with the advantages which the new Act affords their patients, and some doctors have a disinclination towards a procedure that is new to them, preferring to follow the beaten track of certification, which, considering the recent outcry against the dangers of such a course, is not a little surprising. There are those who believe it to be a serious drawback to the efficacy of the Act that it should have insisted on a panel of specially approved practitioners who alone are legally entitled to sign the second recommendation.

A further difficulty is presented by the patient who cannot in the strict sense of the term be styled non-volitional. It seems somewhat invidious that the manic patient should not be allowed to share the benefits of this provision, which the confused or stuporose patient receives. It might have been possible to allow all patients to be dealt with as temporary, provided that they did not actively resist or protest against being sent to hospital. But this is an instance of the necessity for compromise, and it will be time to talk of amendments when the truly non-volitional case is catered for as it now can be.

The Board of Control derives considerable satisfaction from the marked increase of co-operation between the mental hospitals and the voluntary general hospitals by way of their out-patient departments. At the end of 1930 there were twenty-five out-patient departments in which mental cases were examined; by the end of 1931 the number had increased to sixty-one. This progress is most encouraging, and has been mainly due to the sympathetic and assiduous instigation of the Board itself.

England and Wales

Vocational Guidance

A sociological experiment carried out by the Birmingham education authorities in collaboration with the National Institute of Industrial Psychology is described in a report entitled "The value of vocational training as an aid to choice of education."[1] The purpose of the experiment, which was complementary to an earlier one on a larger scale carried out by the Institute in London, was to discover whether scientific tests of a child's "bent" and "aptitudes" formed a more reliable guide to employment than the usual method adopted at the school-leaving conference, where recommendations are based mainly on school reports and the general "impression" of the child gained in an interview. The three hundred boys and girls leaving three elementary schools in Birmingham in 1928 were divided by chance distribution into two groups, one forming the "tested" and one the "control" group. The children in the "tested" group were medically examined, intelligence and other special aptitudes were tested, and a "rating" was made of outstanding temperamental traits. The vocational recommendation was based on these findings. The "control" group was not tested, but advised in the ordinary way at the school-leaving conference. The careers of both groups were observed over a period of two years and their success or failure noted in relation to the advice given. Both groups fall into two subgroups—those who followed the advice ("accordance" posts) and those who did not follow it ("non-accordance" posts). Comparisons were made on a basis of: (1) length of tenure of posts; (2) employers' reports on the children's efficiency; (3) children's reports on the suitability of their work; (4) reasons for leaving posts. All these comparisons strongly indicate the superiority of advice based on tests. For example, in the tested group, 64 per cent. of the children whose first post was in accordance with the recommendation retained it for more than six months; 45 per cent. retained it over eighteen months. Of those entering "non-

[1] Obtainable from the Birmingham Education Committee, Council House, Market Street, Birmingham. (1s.)

accordance" posts 26 per cent. remained more than six months and 12 per cent. more than eighteen months. In the control group these indications are reversed: 45 per cent. retained "accordance" posts for more than six months and 30 per cent. more than eighteen months; while of those in "non-accordance" posts 55 per cent. remained more than six months and 33 per cent. more than eighteen months. Again, of tested children in "accordance" posts, 96 per cent. were reported by their employers to be satisfactory and 44 per cent. "very suitable" (the second group is included in the first); of those in "non-accordance" posts only 42 per cent. were regarded as satisfactory and 14 per cent. as "very suitable." The opinions of the children themselves show the same trend: 90 per cent. of tested children in "accordance" posts report them satisfactory and 38 per cent. as "very suitable," while of those in "non-accordance" posts only 19 per cent. report "satisfactory" and 4 per cent. "very suitable."

Prevention of Tuberculosis

Statistics form a prominent feature of the annual report for 1931 of the council of the National Association for the Prevention of Tuberculosis, which was presented at the annual meeting of that association in July. Since 1871 there has been a progressive decline in the death rate from all forms of tuberculosis in England and Wales, apart from a sharp rise in the war years; the decline has rather slackened during the last five years. The present rate is the lowest which has yet been recorded in this country. All ages and both sexes share in the decline, which is most marked in childhood, but less substantial in young adult life and in old age than at other periods. In Scotland, however, the decline continues without slackening. Special attention is devoted in the report to the progress at Burrow Hill Sanatorium Colony, where the scheme for the combined sanatorium treatment and technical training of youths between the ages of 14 and 19 has been stabilized. The colony regime has become established, the working routine is accepted by patients as a matter of course, and the demands of discipline are met almost without question. Prolonged stay in this institution is now more general, and will, it is hoped, diminish the likelihood of subsequent relapses. Of seventy-eight patients discharged, sixty-two were improved in health and eleven stationary; four were worse, and one patient had died. Since 49 per cent. of the admitted pulmonary cases had tubercle bacilli in the sputum, these results are considered satisfactory. Many of those who have left the institution are engaged in remunerative occupations; in twenty out of sixty-four ex-patients this employment is directly utilizing the training given to them. Another promising side of the work carried on by the National Association is the inquiry into the unduly high mortality from tuberculosis in the Tyneside area. The report states that the house-to-house inquiry and other investigations in that district had been completed by the end of 1931, and the analysis of the data is proceeding. It is hoped to publish a full account of the work with a summary of conclusions before long. The report contains a plea for more energetic and organized propaganda work, so that more effective prophylaxis may be achieved. The lines on which this might proceed are indicated; they include the instruction of care committees, the delivery of popular lectures illustrated by cinematograph films and lantern slides, and the distribution of leaflets and pamphlets.

After-History in Pulmonary Tuberculosis

The sixth survey of the after-histories of patients who received residential treatment under the London County Council's tuberculosis scheme has just been presented to the Council. The particulars give the after-histories of those who were discharged in 1926—that is, six years ago. Patients are divided into two main classes: A (in which tubercle bacilli were not found in the sputum), and B (sputum-positive). The latter class is further subdivided into (1) early cases, (2) moderately advanced, and (3) advanced. The early cases are those with slight constitutional disturbance, if any, and obvious signs of very limited extent. The advanced are those with profound systemic disturbance, or constitutional deterioration, or showing grave complications. The moderately advanced are those which come between these two extremes. During 1926 4,810 adults were discharged from institutional treatment. In 370 the diagnosis was not confirmed, and of the remainder 508 were not traceable. The number of cases, therefore, which has been investigated is 3,932, which includes 268 surgical cases. The mortality records after five years show the following results:

Class	Males		Dead	Females		Dead
	No. of Cases	Alive Five Years after Discharge		No. of Cases	Alive Five Years after Discharge	
Pulmonary		Per cent.	Per cent.		Per cent.	Per cent.
A	244	76.6	23.4	243	75.7	24.3
B (1)	123	65.9	34.1	93	58.1	41.9
B (2)	1,493	28.9	71.1	743	27.5	72.5
B (3)	467	2.6	97.4	258	6.6	93.4
Surgical	140	74.3	25.7	128	83.6	16.4

During the year 1926 882 children were discharged from residential institutions after having received at least one period of residential treatment. Leaving aside 158 cases in which the diagnosis of tuberculosis was not confirmed, 75 in which reports are not available, and 7 in which the patients have died from some other disease, the number of children dealt with in the report is 642. The mortality records show that 140 pulmonary and 421 non-pulmonary cases were still alive after five years, the percentages being as follows:

Class	Total	Alive Five Years after Discharge	Dead
Pulmonary		Per cent.	Per cent.
A	143	89.6	10.4
B (1)	5	20.0	80.0
B (2)	19	52.7	47.3
B (3)	26	3.9	96.1
Non-pulmonary (surgical)	449	93.8	6.2

Prevention of Diphtheria

Satisfactory results of the work done in diphtheria prevention are noted in the annual report of Guy's Hospital bacteriological department just issued. During the past year seventy new cases attended the hospital's diphtheria carrier clinic, of which sixty-four were children of school age. By the end of the year all these "carriers" had been discharged as free from Klebs-Loeffler bacilli. The report gives an account of the highly successful result of Schick testing and immunization in the prevention of diphtheria as applied by the staff of Guy's to boys at an orphanage in Stockwell. During the years 1925–7, inclusive, some thirty-seven cases of diphtheria occurred among the boys. Schick testing and subsequent immunizing of the "positives" was performed in the period October-December, 1927, and applied to new boys as they were admitted. A complete "clean-out" has resulted. Since this date there has not been a case of diphtheria among the boys. The girls at the same institution

were submitted later to the same procedure. Two cases of diphtheria occurred within four months of the completion of the treatment among the immunized girls, and three among new girls who were awaiting a Schick test. Otherwise there have been no cases. All new nurses entering Guy's Hospital during the past four and a half years have been Schick-tested, and if "positive" immunized. Before this test was instituted eighteen cases of diphtheria occurred among the nurses in six months. During the four and a half years since the regulation came into force the total number of cases among the nurses has been only eighteen.

Ireland

Milk Supply in Belfast

Dr. C. S. Thomson, superintendent medical officer of health, Belfast, has forwarded to the members of the Public Health Committee a copy of a letter which he has sent to the Ministry of Home Affairs. In the course of the letter Dr. Thomson reminded the Ministry that he wrote to them on May 11th last in connexion with tuberculous infection of milk supplies. The object of the committee, the letter continued, was that effect be given to the recommendations regarding Belfast's milk supply—namely, that only Grade A (T.T.) and pasteurized milk be sold in the city, and that one year's notice be given to milk vendors of the requirements of the corporation in this respect. Dr. Thomson's letter to the Ministry also drew attention to a report issued by the subcommittee, set up under the chairmanship of Dr. W. G. Savage, medical officer for Somerset, to consider the available methods for combating tuberculosis of bovine origin. This report expressed the opinion that the time had now come when pasteurization should be adopted on a larger scale. To this end, Dr. Thomson's letter added, it was suggested that the Ministry of Health should draw up milk regulations for adoption by the larger urban authorities, requiring (1) that all milk sold within the jurisdiction of the authority should either come from tuberculin-tested herds or be effectually pasteurized; (2) that no milk treated by heat, other than by the official process of pasteurization, should be imported into the area; (3) that there should be compulsory classification of all grades of milk sold within the area; and (4) that adequate supervision and control over the health of all persons engaged in the production and distribution of milk should be secured.

Free State Medical Registration Council

Nominations for the office of registered medical practitioners as direct representative members of the Medical Registration Council were received on August 13th. As only two nominations were sent in to fill the two vacancies an election was unnecessary, and the returning officer, Dr. Denis J. Coffey, President of the Council, declared the nominated candidates, Mr. William Doolin, M.B., F.R.C.S.I., 2, Fitzwilliam Square, Dublin, and Dr. R. J. Rowlette, M.D., F.R.C.P.I., 55, Fitzwilliam Square, Dublin, to be the direct representative members of the Council.

Royal Victoria Hospital

At the bi-monthly meeting of the board of management of the Royal Victoria Hospital, Belfast, Colonel A. B. Mitchell, F.R.C.S., presiding, it was stated that the Hospital Saturday collection had been the means of raising £72,000 for the hospital since it was first undertaken in the year 1884. The superintendent reported that the amount received to date from the collection was £3,250, and when the returns from a few country districts were received the total would be about £3,800. The board of management expressed itself as gratified by the success of the collection, and offered its heartiest thanks to the honorary secretaries, superintendents of districts, collectors, members of the working men's committee, the Press, the manager of the Belfast City Tramways, and to all who helped to make the collection such a success. The honorary treasurer reported the receipt of various other donations.

Hospitals' Share of Sweepstakes

The Free State Department of Justice has issued the following statement: Repeated references have appeared in the Press to the delay in distributing the hospitals' share of the proceeds of sweepstakes. The facts of the matter are as follow: the Public Charitable Hospitals Amendment Act, 1931, provided that a committee of reference should inquire into the needs and circumstances of institutions participating in the proceeds of sweepstakes and report to the Minister as to the manner in which the proceeds should be allocated. The responsibility for the distribution rests on the Minister for Justice, but he is bound by the Act to consult with the Minister for Local Government and Public Health before he gives his final decision. The Minister's anxieties in the matter are to secure: (1) that a fair distribution will be made amongst the hospitals, and (2) that the moneys so distributed will be used to the best possible advantage. The report of the committee requires very careful consideration, not merely in the Department of Justice, but also in the Department of Local Government and Public Health, and such consideration could hardly be expected to be completed in a short space of time. Moreover, a complaint was received from one of the participating institutions that the committee, in dealing with their case, adopted an unfair basis, and that, as a result, the amount recommended was inadequate. This complaint requires attention, and it will not be possible until a decision has been reached as to the merits of the dispute for the Minister to give instructions as to the final distribution of the available surplus. It will be appreciated that if the distribution recommended by the committee is altered in respect of one institution, corresponding adjustments must be made in respect of other institutions. As, however, it was alleged that certain institutions were being prevented from proceeding with necessary works, the Minister recently directed that one-third of the amount recommended by the committee should be paid out in each case. The balance will be distributed when he has come to a decision as to whether the committee's recommendations require alteration to meet the case of the institution which has lodged a complaint. On the question of urgency, which has been repeatedly referred to in the Press, and the holding up of building works with consequential loss of employment, attention is drawn to paragraphs 39 to 42 of the Committee's report, in which they state that extensive building operations should be discouraged and postponed. They go on to point out that building programmes are apt to be hastily conceived and carried out without close and expert study of the special problems involved. In another part of the report they mention the case of one institution, which, having regard to its situation, appears to offer no promise of being adapted to the current trend of hospital development, and they suggest that it would be desirable that the institution in question should be removed to another site. For these reasons the Minister is satisfied that it is advisable that institutions should proceed with caution, and that they should await the development of sweepstakes, so that they may be able to form a reasonable estimate of the total sum which they are likely to receive before embarking on ambitious enlargements. The

committee of reference is at present occupied with the consideration of the distribution of the proceeeds of sweepstakes subsequent to the Manchester November Handicap, 1931, and no distribution in relation to such sweepstakes can be made until the committee's reports are received.

Correspondence

BLOOD TRANSFUSION

Sir,—The article by Mr. A. M. A. Moore in the *Journal* of July 23rd and Mr. J. B. Oldham's letter in that of August 13th have again drawn attention to the technique of obtaining blood from a donor. The blood donor is usually a young and healthy individual who wishes to return to his occupation at once, and his interests deserve every consideration. I agree, therefore, that the process should be painless, and that novocain (or "novutox") should always be used. Mr. Oldham adds, however, "a considerable amount of force is sometimes necessary to push a large-bore venesection needle through the skin," with occasional injury to the vein and extravasation of blood. The necessity for this force seems to me to constitute an error in technique which should be eliminated. Everyone who performs transfusions frequently will evolve his own technique, and for many years I have used the following device:

In the small area of anaesthetized skin over the distended vein a tiny nick is made with the point of a scalpel. This is not more than 2 mm. in length and is just sufficient to accommodate a large-bore needle such as French's. The vein is not exposed. A fine half-curved round-bodied needle is then introduced at the upper end of the nick, made to transfix the *anterior* wall of the vein, and brought out again through the skin. The transfusion needle is then introduced *under* the transfixing needle. No force is needed, and the lumen of the vein cannot be missed. The manœuvre is quite easy after a little practice, and eliminates all risk of injury to the donor.

The process is very well shown in detail in the blood transfusion film made by Messrs. Kodak for their medical film library. This film was made partly for the use of the London Blood Transfusion Service, organized by Mr. P. L. Oliver, O.B.E., and now incorporated in the British Red Cross Society. The volunteer donors of this Service are instructed to refuse to allow their veins to be exposed by dissection, several instances of subsequent disability having followed such a process. With the growing importance of blood transfusion as a therapeutic measure, and the spread of voluntary donor organizations, these small points in technique become increasingly important.—I am, etc.,

London, N.W.1, Aug. 18th. Geoffrey Keynes.

THE ORIGIN OF TUMOURS

Sir,—Mr. Lockhart-Mummery declines to answer my question. He has now shifted his position. His first explanation of the non-cellular transmission of fowl tumours—namely, that filtrates contain invisible particles of chromosomes which are able to grow again into whole cells—has the merit of simplicity and definiteness. Now he has adopted the vague hypothesis supported by Dr. des Ligneris, according to which a filtrate contains an indefinite, unknown, invisible portion of a cell which grows again into a tumour cell. The chromosome explanation, by the way, was originally offered as an easy solution of Dr. des Ligneris's difficulties.

It is evident from Mr. Lockhart-Mummery's letter that he lacks the exact knowledge of filterable tumours which comes only from work at the bench.

A tumour filtrate is made by pounding tumour tissue in the presence of sand and then extracting the mass with saline, which, after it has been spun to throw down sand and tissue débris, is filtered through a bacteria-proof candle such as the Berkefeld N. The filter removes even the smallest bacteria and all particles of that order of size. It has now been shown by filtration through collodion membranes of differing porosity that the active "agent" in the filtrate is of the order of size of 0.1 micron.

Now in his letter in the *Journal* of August 20th Mr. Lockhart-Mummery refers to certain experiments on regeneration in lowly organized animals as if the filtration methods employed in those experiments—the animals were simply squeezed through bolting cloth or silk—were comparable with those employed in the study of fowl tumours. They are not relevant. When the hydrozoan *pennaria* is squeezed through silk, cells and groups of cells pass through the fabric and regeneration from groups of cells takes place; in tumour filtrates there is not one cell, or even a visible portion of a cell. If Mr. Lockhart-Mummery could give us an instance where an animal can be disintegrated, extracted with a fluid, and the fluid then passed through a Berkefeld N candle to yield a filtrate from which the animal could be regenerated, then I am sure most scientific workers would sit up and take notice. There is no such instance, of course, and the enumeration of relatively coarse experiments on regeneration is beside the point.

When tumour tissues are dried the minced tissue is put into a desiccator in which trays of phosphorus pentoxide are stacked, and the desiccator is evacuated by means of a good mechanical pump. If the pump is kept running for an hour the rate of loss of water is increased, and the activity—that is, the tumour-producing power—of the dried tissue is enhanced. After evacuation the desiccator is closed, and the tissue is allowed to remain *in vacuo* over phosphorus pentoxide for several days. The tissue is then taken out and powdered in a sterile mortar. The powder is placed in test tubes, which are then kept over P_2O_5 *in vacuo* for several weeks. Finally, the tubes are sealed in a flame and stored, usually in the ice-box. Tumour tissue dried in this way remains active for years.

Now there is a quantitative aspect of the process of desiccation which has not, so far as I am aware, received adequate attention. What proportion of water remains in tumour tissue which has been treated in the manner described? I do not know, but it is not hazardous to suggest that the amount is certainly a fraction of 1 per cent. We know that some viruses withstand drying by this method. Can Mr. Lockhart-Mummery tell us of any animal or animal cell which can be desiccated in this way and remain alive even for twenty-four hours? Of course he cannot. His reference to *clavellina* is again beside the point at issue.

But even if an example of the reconstitution of a cell from an ultramicroscopical particle of a chromosome, or from indefinite, unspecified, ultramicroscopical parts of a cell, could be produced, the application of the example to the problem of filterable tumours would be dangerous, and would lead to greater difficulties than the virus theory. For example, it would be necessary to explain how it comes about that a tumour like Mill Hill No. 1, a fibrosarcoma, can give rise to circulating antibodies which neutralize not only the agent of the fibrosarcoma, but also the agents of the Rous tumour and the endothelioma Mill Hill No. 2. We should have to suppose that during the growth of the fibrosarcoma the hypothetical parts of the cell break off and find their way into the blood stream of the host; then we should be compelled to say that a fowl makes an antibody to parts of its own cells very easily, and we should have to seek for the mechanism which protects normal cells of the fowl against the action of this antibody. Next, we should have considerable difficulty in explaining the neutralization of the agents of the other histologically different tumours. Again, we

should find it difficult to understand how the ultramicroscopical parts of the cells of Fujinami's fowl tumour are able to grow into whole cells in the duck, especially as the cells of the duck tumour are duck and not fowl cells. The formation of complete duck cells from the invisible particles of a fowl cell would be a very remarkable phenomenon. These are but a few of the difficulties which would confront Mr. Lockhart-Mummery's theory, even if, to begin with, he could produce facts which would justify an *a priori* case for investigating or even considering his theory. But there are no such facts.

The chromosome explanation is now abandoned, and may be left at that; but I should like to ask Mr. Lockhart-Mummery a definite question which is worthy of a definite answer: Does he really think that an ultramicroscopical particle of a cell can grow again into a whole cell?—I am, etc.,

Mill Hill, Aug. 21st. W. E. GYE.

THE LUNGS IN ANAESTHESIA

SIR,—The discussion on the care of the lungs in anaesthesia, opened by Dr. Featherstone at the Centenary Meeting in the Section of Anaesthetics, raised many interesting points. I am in complete agreement with his statement that anoxaemia should be avoided studiously. The hectic form of anaesthesia in which the patient is partially cyanosed is more likely to produce unpleasant pulmonary sequels than any other. I think that in the past we have been too prone to regard oxygen as an emergency remedy instead of an important adjuvant to the anaesthetic. With regard to the choice of an anaesthetic, I believe that it is of less importance to choose the drug which is least irritant to the respiratory apparatus. Often the best drug by the inhalation method is that which will produce the maximum muscular relaxation and so enable the surgeon to perform his abdominal section with speed and minimum violence, for, as Crile has shown, heavy-handed manipulation of the peritoneal surfaces can produce temporary inhibition of the diaphragm, resulting in defective aeration of the lung bases and subsequent collapse. Of course, spinal anaesthetics produce admirable relaxation, but in high abdominal operations the intercostal paralysis lasts too long.

I notice that some speakers advocated the use of carbon dioxide as a preventive measure against post-anaesthetic chest complications. I freely admit its value at the end of the operation (even then I think it should be warmed), but I do doubt the wisdom of using it combined with oxygen throughout the anaesthetic. Some authorities advocate the use of a mixture of 95 per cent. oxygen with 5 per cent. carbon dioxide, and such a mixture is obtainable commercially.

Before suggesting a possible danger, I would recall a familiar fact. Pavlov caused young puppies to breathe an atmosphere of pure oxygen, and by so doing produced collapse of the lung. Now, theoretically speaking, what is the effect of the prolonged use of an oxygen-carbon-dioxide mixture? The carbon dioxide causes an increase in the ventilation of the lungs, and by so doing washes out the inert gases of the "dead space," replacing them by something approximating to 95 per cent. oxygen. Ultimately by diffusion this permeates the alveoli. At the end of a long administration the oxygen is absorbed rapidly, the alveolar walls fall together, and this originates a pulmonary collapse of the type that Pavlov produced. I admit that this is pure theory, yet I have known one case of extensive pulmonary collapse following the prolonged use of such a mixture, and I advance this view in the hope of eliciting the experience of others.—I am, etc.,

L. T. CLARKE.

Queen's Hospital, Birmingham, Aug. 16th.

ANAESTHESIA IN LABOUR

SIR,—In your review of the Final Report of the Departmental Committee on Maternal Mortality and Morbidity I am interested to find so much commendation of the attitude taken by the Dutch in regard to the use of anaesthetics in midwifery. The administration of anaesthetics in normal labour is condemned by the Dutch, who say that the natural processes tend to be retarded thereby and artificial aids to delivery are in consequence a necessity. As one who has had a very wide experience of the use of sedatives and anaesthetics in labour, I can affirm that under careful management the use of sedatives and anaesthetics in so-called normal labour has a most beneficial effect.

Suffering is prevented to a great extent and the course of labour is not retarded. Shock is prevented, and as a consequence the incidence of puerperal sepsis is diminished. Gas and oxygen, when given in the second stage, not only relieve pain but stimulate uterine contractions. In domestic practice the use of chloroform in small and intermittent doses in the second stage diminishes suffering to a very great extent. In discussions which take place on this subject from time to time it is generally assumed that the partisans of those methods which might be termed "humane" advocate the prolonged drenching of patients in a general anaesthetic. In these discussions little light is thrown upon the practical side of the matter of sedatives for the reason that only a small number of medical practitioners appear sufficiently interested to study the question thoroughly. Research upon the use of sedatives, especially in the first stage of labour, cannot fail to lead to good results. It is a pity that the efforts made by those who are prompted by a sincere desire to relieve suffering should be discouraged and referred to by you as "misdirected," more especially as considerable financial assistance has been provided for such research. The question has now to be faced seriously.

The report (page 43) refers to the experiments being made at maternity hospitals. To those of us who have for years employed methods for the relief of pain the merely experimental stage is long past, and we have had convincing proof of the efficacy and advantages of sedatives and anaesthetics in what we are still pleased to call normal labour. We must still continue researches into the character of new methods and new drugs. A further argument is that women themselves nowadays universally demand relief from suffering. This may be the result of education and the modern tendency to avoid discomfort of any sort.

I speak only from my experience of women in this country. I know nothing of the temperament of the Dutch. This factor may be of some importance when expressing an opinion based upon experience.—I am, etc.,

Royal Free Hospital, Aug. 17th. A. LOUISE MCILROY.

ASSOCIATION OF ANAESTHETISTS OF GREAT BRITAIN AND IRELAND

SIR,—At a meeting of about seventy anaesthetists, held in London on July 1st, a new independent society of anaesthetists was formed. The object of the association is "to promote the development of this branch of medicine."

Anaesthetists "who are engaged either in the teaching of anaesthetics at the schools of medicine and hospitals recognized by the University of Cambridge or in research in Great Britain and Ireland" are eligible for election to membership, which is limited to 150.

At the inaugural meeting, by resolutions which were unanimous, ninety-five members were elected, rules were passed, and a council of sixteen members was formed. The council is composed as follows:

President: H. W. Featherstone (Birmingham), 54, Newhall Street, Birmingham. *Vice-President*: Joseph Blomfield (St. George's). *Honorary Secretary*: W. Howard Jones (Charing Cross), 43, Cambridge Street, Hyde Park, W.2. *Honorary Treasurer*: Z. Mennell (St. Thomas's), 149, Harley Street, W.1. *Other Members of Council*: R. E. Apperley (Middlesex), H. E. G. Boyle (St. Bartholomew's), J. H. Chaldecott (St. Mary's), Ashley S. Daly (London Hospital), H. P. Fairlie (Glasgow), A. L. Flemming (Bristol), C. F. Hadfield (St. Bartholomew's), E. Falkner Hill (Manchester), Cecil Hughes (King's College Hospital), J. Ross Mackenzie (Aberdeen), G. Ramsay Phillips (St. Mary's), and H. Torrance Thompson (Edinburgh).

Anaesthetists who desire to apply for membership should communicate with Dr. W. Howard Jones, 43, Cambridge Street, Hyde Park, W.2.—I am, etc.,

Henry W. Featherstone,
Birmingham, Aug. 15th. President.

INJECTIONS OF OXYGEN

Sir,—Oxygen has been injected into various tissues, often with beneficial results. Recently Dr. Welsh referred to rapid relief of anoxaemia following subcutaneous injection of oxygen. For some years such injections have also been employed by Bayeau and others in France. Beneficial results have also been recorded following injections into the stomach. The explanation usually given for these results—namely, that the oxygen injected is rapidly absorbed and increases the saturation of the blood with oxygen—is erroneous, as physiological research has shown. What, then, is the explanation? I have been studying oxygen tensions in the tissues for about ten years, and normally these tensions lie between 10 and 40 mm. Hg in all regions examined, except in the intestine with food present and fermentation proceeding, when the oxygen tension falls below 10 mm. Hg.

In the subcutaneous tissues, peritoneal cavity, pleural cavity, urinary bladder, gall-bladder, uterus, cleaned-out lumen of the small intestine, and lateral ventricle of the brain, the normal oxygen tensions lie between 20 to 40 mm. Hg, and the normal carbon dioxide tensions between 35 and 60 mm. Hg, nitrogen tension being about 570 mm. Hg, and water vapour 47. The tensions in the lateral ventricle of the brain have been obtained recently by injecting only a small bubble of gas and by analysing, after some hours, by a modification of Krogh's micro-method. In the mucous membrane of the cleaned-out stomach the oxygen tension is about 10 to 20 mm. Hg, and the carbon dioxide tension about 35 to 60 mm. Hg.

When pure oxygen is injected into any of the above regions the oxygen tension becomes immediately increased to about 760–47 (for water vapour), or 713 mm. Hg, and at the same time the tensions of nitrogen and carbon dioxide become greatly decreased. Of course carbon dioxide soon diffuses out rapidly from the tissues until its tension in the free gas becomes 35 to 60 mm. Hg—that is, the same as in the surrounding tissues. The oxygen and nitrogen tensions require much longer—several days—to become adjusted. Immediately after the injection there is an eighteen-fold increase in oxygen tension—that is, from the normal 40 to 713 mm. Hg. This probably causes reflex effects such as increase in depth of breathing, which would explain the immediate relief of anoxaemia in the patients. The injection also causes injury or mechanical changes in the tissues, and this may also produce similar reflex effects; in this case beneficial results should follow injection of nitrogen as readily as with oxygen.

Beneficial effects following injection of oxygen per rectum for certain types of colitis have been recorded by American observers. In this case the oxygen inhibits the growth of anaerobic bacteria and perhaps also benefits injured mucous membrane lacking oxygen owing to pathological changes.—I am, etc.,

J. Argyll Campbell.
National Institute for Medical Research,
Hampstead, Aug. 16th.

SACRO-ILIAC SUBLUXATION

Sir,—I was surprised to note that in your review of Mr. Walter Mercer's textbook of orthopaedic surgery, in your issue of July 16th, exception was taken to the fact that so-called sacro-iliac subluxation received so little attention. That this surprise was well founded is borne out by these words occurring in your issue of August 6th, in the review of Barker and Trescher's monograph on backache:

"Of sacro-iliac subluxation—a diagnosis *not long ago* as frequently made in the United States as it was rarely in England—the authors write that 'it is now believed to occur *less often than was formerly supposed*.'" (The italics are mine.)

Your reviewer suggests that British surgeons who were, in the main, unable to substantiate or support the American claims will be accordingly relieved.

There seems to be a distinct tendency for some British workers to adopt everything new and spectacular in surgery, but I would suggest to your reviewer that the absence of such ethereal diagnostic flights as so-called sacro-iliac subluxation from responsible textbooks should not be held up in cold print as shortcomings.

The anatomical position of the sacro-iliac joint and the method of its protection are such that definite subluxation at this joint must be an occurrence of great rarity. A review of the literature on the subject indicates quite clearly that the unfortunate term "subluxation" has been inaptly applied to a condition of sacro-iliac sprain, which receives adequate notice both in Mr. Mercer's textbook and in Jones and Lovett's classical work.—I am, etc.,

Edinburgh, Aug. 17th. James Fleming, M.B., Ch.B.

PATHOGENESIS OF IDIOPATHIC HYDROCELE

Sir,—The recent correspondence on the aetiology of hydrocele (August 13th) prompts me to put forward my own experience. Twelve years of contact with genito-urinary out-patients has given me a special opportunity of seeing a large number of cases suffering from this condition.

I have been specially interested in finding a cause for the collection of fluid within the tunica vaginalis, and have always made a point of carefully palpating the corresponding testicle and epididymis; when operation has been perfomed I have taken the opportunity of carefully inspecting these organs. I can recall no case in which pathological changes in the epididymis were not easily palpable or visible. In the great majority I would go so far as to say that these were gross. Quite commonly the epididymis was enlarged, hard, and adherent to the testicle. In cases submitted to operation the changes were, as a rule, not so marked, doubtless because these patients were on the whole younger than the others.

I have always looked upon these changes in the external genitals as part of a generalized process throughout the whole genital system (which often involved the urinary tract as well), and due to an infection acquired in the past—not necessarily gonococcal. Accompanying the external genital changes one finds any degree of inflammation, not only of the internal genitals, but also of the bladder-neck

The cases of epididymitis giving rise to hydrocele as the first striking evidence that hypertrophic changes are taking place in the prostate form an interesting clinical group. These have always impressed me with the fact that simple enlargement predisposes, in some cases at least, to infection in the gland.

Most interesting of all the hydrocele cases are those with which I have come in contact in young children. As a member of the honorary surgical staff of the East London Hospital for Children I have had facilities for seeing and investigating a number of these. I have never failed to find in any of them evidence of infection in either the testis or the epididymis as soon as these organs have become palpable. My knowledge of the widespread distribution of signs of infection throughout the genital system in the same cases in adults has caused me to look for these changes in children. These investigations have revealed a number of cases of acute and chronic prostatitis which otherwise would have escaped detection. One cannot help feeling that infection of the internal genitals in cases of hydrocele in children is not only generally overlooked, but is very rarely considered as a possibility.—I am, etc.,

London, W.1, Aug. 13th. H. P. Winsbury-White.

ARTHRITIS AND DENTAL SEPSIS

Sir,—There is a somewhat remarkable parallel between two bone diseases which may be thought of interest. In dental caries (as has been pointed out by Dr. E. W. Fish), even when the rest of the teeth are very considerably affected, the six lower incisors remain in good condition in practically all cases. In rheumatoid arthritis, which enlarges and distorts all the other limb joints in the body, the distal phalanges of the eight fingers and toes tend either to remain untouched or to be less severely injured than the neighbouring joints. On the other hand, pyorrhoea and osteo-arthritis respectively do attack these special areas as readily as any others. In view of the facts to which Dr. F. W. Broderick draws attention in your issue of November 7th, 1931, where, besides comparing the age incidence of the four diseases, he notes the association of acidity with caries and with rheumatoid arthritis, and of alkalinity with pyorrhoea and with osteo-arthritis, it is interesting to find a further point of similarity between these diseases. The coincidence is the more striking because it seems so extraordinary that these particular places should escape damage, either in the one disease or the other.—I am, etc.,

Bath, Aug. 13th. "Crippled."

CORONARY THROMBOSIS

Sir,—At the meeting of the Section of Medicine on July 28th, reported in your issue of August 13th, our positive knowledge of coronary thrombosis was summarized. Not only was the pain of angina (relieved by cessation of effort and by nitrites) differentiated from that of the sudden organic lesion (relieved only by opium), but the two were linked up to a common cause—ischaemia (lucidly explained by Sir Thomas Lewis). As to prognosis and treatment great stress was laid on prolonged rest in bed, five weeks being an agreed minimum, while some advocated three months ; instances were cited of patients who had disobeyed, got up, and promptly died. Incidentally it was mentioned by two speakers that coronary thrombosis might occur without pain, though this was not emphasized or discussed.

That we have by no means reached full knowledge of the subject is suggested by the fact that patients have disobeyed orders and got up, not only without incurring the immediate penalty, but with rapid convalescence proceeding sometimes to apparently perfect health and leaving no trace of cardiac mischief either clinically or in the eventual electrocardiogram. Yet such patients may have a sclerosed patch and possibly an aneurysm of the heart wall. Indeed, the history of patients who die of ruptured cardiac aneurysm may be entirely free from any kind of ill-health whatever until the final catastrophe. The post-mortem examination of such hearts may show unmistakably that the lesion was by no means a recent one ; yet all must have started in the blocking of a coronary area with, in these cases, no initial symptom of distress, no subsequent ill-health in spite of complete disregard of precautions, and with ability to live a strenuous life (one was a dock labourer) to the end.[1] [2]

These considerations suggest that coronary thrombosis may be a good deal commoner than the record of recognized cases accounts for, and that apparent recovery is not necessarily dependent on prolonged recumbency. Such cases are unsuspected and would seem to be quite undiagnosable, though routine records of apparently healthy hearts may perhaps catch some in the characteristic phase illustrated by Dr. Bedford at the meeting, and well known for some time past to those interested in electrocardiography.—I am, etc.,

Claude Wilson, M.D., M.R.C.P.

Tunbridge Wells, Aug. 14th.

ERGOSTEROL AND HYPERTENSION

Sir,—In a recent investigation, covering a period of ten years, which I carried out on a series of cases of hypertension in a country practice, my attention was drawn to the number of these cases which gave a " gall-bladder history " (gall-stones, cholecystitis, biliary colic, etc.).

I have now searched the literature and find several references to the occurrence of hypercholesterolaemia in hypertension, but none of the investigators is inclined to believe that cholesterol is the cause of hypertension. The recent discussion on cholesterol metabolism in disease by the Section of Pathology at the British Medical Association Centenary Meeting and summarized in the *Journal* of August 13th gives further evidence on this question. A very interesting point, however, arises. Fowweather, in *A Handbook of Clinical Chemical Pathology*, states that " ergosterol is present in small quantities along with cholesterol (about 1 in 2,000) from practically all sources, and is only separated from it with difficulty." Is it possible, then, that the incriminating factor in hypertension is the ergosterol which is in constant association with the cholesterol?

The persistent increase of ergosterol in the blood, with its ergot-like action, would have a continuous tonic action on the fine arterioles, slowly leading to hypertrophy of the walls of these vessels and the usual concomitant train of events—raised blood pressure, cardiac hypertrophy, arteriosclerosis, etc. This suggestion that ergosterol may be the root cause of hypertension has not, as far as I know, been previously stated, but I feel that it is worthy of further investigation, and if there is anything in the theory, a whole field for further investigation may be opened up—namely, the question of the ergosterol content of the various foods and the limitation of the " worst offenders " in the prevention of hypertension, also the danger of going too far in prescribing concentrated vitamin foods, and so on.

I have very little biochemical knowledge, but have merely tried to associate my ordinary reading with clinical observations made in general practice.—I am, etc.,

Robert Dawson, M.A., M.D.

Middleton-in-Teesdale, Aug. 15th.

[1] Wilson, C.: *Lancet*, 1919, August 2nd.

[2] Moor, Frewen, and Rogers, Herbert: *British Medical Journal*, August 6th, 1932, p. 241.

PROSTATECTOMY

Sir,—In the *Journals* of August 6th and 13th there is a very full report on the interesting discussion on suprapubic prostatectomy, introduced by Mr. Swift Joly.

For some years we have been using the method of open dissection for tonsils, and it appeared to me that we could excise the prostate as easily and with less damage by tearing if we removed it from its bed by open dissection in a similar manner as in myoma uteri.

I do not have much opportunity of performing the operation, and as no one mentioned this method in the discussion as reported I should be obliged if someone with more opportunity of encountering difficulties would mention what these are.

The only real difference we make is in putting in the retractor immediately after opening the bladder vertically. The patient is put in three-quarter Trendelenburg position, the bladder opened, the retractor inserted, the broad stitch on either side of the bladder wall tied to the retractor, and the bladder and prostate inspected. The prostate is then seized with vulsella behind the urethral opening and pulled gently forward. Dissection with blunt scissors curved on the flat is begun behind or at the side of the vulsella, the line of cleavage is opened, and the prostate gradually freed from its bed. Bleeding points are seen and caught as they appear, as the view is always kept clear by a suction tube. The urethra is cut across with scissors, and any bleeding in this area, sometimes fairly profuse, is stopped. Fine catgut ligatures are used, and no suturing. All bleeding is stopped before the retractor is slowly closed, and any oozing that may occur thereafter will stop with pressure. There are practically no ragged edges, as bands are cut across.

I think that in this open dissection bleeding is less severe than when the prostate is removed with the finger guided by touch alone, and I should be glad if anyone who has tried, and perhaps given up, the open method will expose its pitfalls.—I am, etc.,

Ashford, Kent, Aug. 16th. A. Victor R. Don.

"HISTORY OF THE ASSOCIATION"

Sir,—Doubtless neither yourself nor the committee responsible has failed to receive congratulation on the publication of the *History of the British Medical Association, 1832–1932,* so ably compiled by Mr. E. Muirhead Little. Being one of the fortunate 4,000 who attended the Centenary celebrations, my presentation copy of the *History* is highly appreciated as a worthy souvenir of an exceptional event. Apart altogether from such consideration, the contents of the book appear to be as complete as is possible, the gradual development of the Association, effectively portrayed, abounds in interesting facts, and the evaluation of the many phases of the Association's work is carefully balanced and clearly stated.

The type is a delight to read—even for a forty to fifty years' member—and the general format distinctive and convenient. The illustrations, both personal and pictorial, are well worth inclusion in this notable volume. One regret only assails the mind in the perusal of some of the striking photographs—of those with whom one can recall happy experiences of friendship and guidance, and who have indeed served their day and generation faithfully, but are no longer with us. Everyone interested in past and present activities of the British Medical Association will value such a comprehensive record, and it is good to note that the *History* can now be obtained by those who were unable to attend the Centenary Meeting.—I am, etc.,

Burgess Hill, Sussex, Aug. 17th. W. W. Shrubshall.

Obituary

GUSTAVE MONOD, M.D.Paris, F.R.C.P.Lond.

Our *entente médicale* with France has lost its best liaison officer by the death of Dr. Gustave Monod of Vichy, and the many British visitors to that spa have lost a wise physician and a kind friend. He belonged to one of the largest and best-known professional "clans" in France. Members of that family are to be found throughout that country, and also in Canada, holding good positions in the law, medicine, and the Church. The latter was the "Reformed Protestant" or Waldensian Church, and although those holding this faith are in a minority in France this never proved a bar to the rise of the Monod family to distinction and success.

Dr. Monod smoked rarely and was a teetotaler. The writer of this notice once asked him which wine he recommended most and which he thought the most harmless. His reply was: "You know I think everyone is better with no wine at all. If you must drink wine, be sure you drink good wine. The least harmful is probably a sound champagne." This was, whatever we may think of it, an unexpected reply from a Frenchman. Monod not only enjoyed a wide acquaintance with the profession in his own country, but almost certainly had more friends in England than did any of his compatriots. This was attributable both to his command of the English language and to his sympathy with the British character and point of view. These two acquirements were frequently illustrated in the Paris Letter, which he was in the habit of contributing to these pages, while his knowledge of our language, as well as his general culture, were well shown by the address on Pasteur as an artist, which he gave at one of the soirées of the Royal Society of Medicine. As is well known, considerable importance is attached in France to academical or official recognition. That Dr. Monod's position was well appreciated is shown by the fact that he was entrusted by the Faculté de Médecine of the University of Paris with the work of maintaining contact with the profession in this country, and by his qualification to wear the rosette of Officier de la Légion d'Honneur.

He was a great worker in his own practice, in medical research and literature, in the maintenance of friendship between France and England, and in furthering the welfare of the town of Vichy, for which he did so much. It was doubtless largely a result of a too strenuous devotion to these manifold interests that his death from angina pectoris took place, at a comparatively early age, after five days of intermittent suffering bravely endured.

The late Editor of the *Journal,* Sir Dawson Williams, was a good friend of his, and Monod paid a high tribute to him in an obituary appreciation which he wrote for these columns in 1928. Last year Monod was elected a Fellow of the Royal College of Physicians of London, being the only French physician to hold the Fellowship, which is, indeed, rarely bestowed outside the United Kingdom. This distinction alone—one which greatly pleased him—is sufficient to demonstrate the esteem with which he was regarded in England.

In Vichy he will be regretted, not only by his large clientele of British patients, but also by the medical advisers who transferred them to his care with every confidence. Though no great sportsman, Monod's genial presence will be missed on the golf links alongside the river Allier, as well as in his adjoining villa, where he dispensed a charming hospitality. Madame Monod also belonged to a well-known Waldensian family, and much sympathy must be felt for her and her two little girls.

StC. T.

We regret to record the death, in his seventieth year, of Dr. Thomas Messenger of Kirkbride, Cumberland, a member of an old Cumberland yeoman family which has resided in the Holme Cultram Abbey district for generations. Educated at St. Bee's School and at the University of Edinburgh, he qualified in 1894 with the diplomas of L.R.C.P. and S.Ed. and L.R.F.P.S.Glas. He had practised at Kirkbride for over thirty years, and was held in great esteem by his patients and friends. He was medical officer and public vaccinator for the Bowness District of the Wigton Union, and medical officer to the Post Office, in addition to being medical referee to several assurance companies. He was a member of the Cumberland Division of the British Medical Association. The funeral service at Kirkbride Churchyard, on August 14th, was conducted before a large congregation of friends and patients by the Rev. G. Nedham and Canon Walker of Causewayhead. Dr. Messenger is survived by his widow and one daughter, who is a member of the medical profession.

Universities and Colleges

UNIVERSITY OF LONDON

Applications for the William Julius Mickle Fellowship must be sent in before October 1st. The Fellowship is of the value of at least £200, and is awarded by the Senate to the man or woman who, being a resident in London and a graduate of the University, has in its opinion done most to advance medical science during the preceding five years. Further particulars can be obtained from the Academic Registrar.

UNIVERSITY OF DUBLIN

Trinity College

The usual three weeks' post-graduate course will be held from September 12th to October 1st. The classes will be arranged on similar lines to those held in previous years.

The Services

LEISHMAN PRIZE

Major D. T. Richardson, M.C., Royal Army Medical Corps, has been awarded the Leishman Prize (Officers) for the year 1931, consisting of a silver medal and a sum of £30, for his work in the interests of military hygiene. The Leishman Prize (Officers) is awarded annually for the best piece of work in any branch of medicine, surgery, or allied science, or in connexion with the general duties of the Royal Army Medical Corps, by an officer of the Royal Army Medical Corps, or Army Dental Corps, or by an officer removed from either of these Corps but still on the Active List.

NORTH PERSIAN FORCES MEMORIAL MEDAL

Dr. Neil McLean, Colonial Medical Service, has been awarded the North Persian Forces Memorial Medal for the year 1931 for his paper on "A sleeping sickness investigation in the infected areas of Kavirondo (1930–1931)," published in the *Kenya and East African Medical Journal* of October, 1931. The North Persian Forces Memorial Medal is awarded annually for the best paper on tropical medicine or hygiene published in any journal during the preceding twelve months by a medical officer, of under twelve years' service, of the Royal Navy, Royal Army Medical Corps, Royal Air Force, Indian Medical Service, or of the Colonial Medical Service, provided the Memorial Committee considers that any of the papers published has attained a standard of merit justifying an award.

TERRITORIAL DECORATION

The Territorial Decoration has been conferred on Lieut.-Colonel H. T. Bates, O.B.E., R.A.M.C., T.A., under the terms of the Royal Warrant of October 13th, 1920.

Medical News

The Fellowship of Medicine and Post-Graduate Medical Association announces that a special week-end course in clinical surgery will be given at the Royal Albert Dock Hospital on September 3rd and 4th. From September 5th to 10th there will be an all-day course in diseases of the chest at the Brompton Hospital. A course in psychological medicine will be held at the Bethlem Royal Hospital on Tuesdays and Fridays at 11 a.m. from September 6th to 30th. There will be a course in infants diseases at the Infants Hospital from September 12th to 24th, during the afternoons. From September 12th to 24th there will be a course in ophthalmology at the Royal Eye Hospital—afternoons only. Individual clinics are available daily. Direct arrangements for attendance must be made with the Fellowship of Medicine. All courses of instruction, clinics, etc., arranged by the Fellowship of Medicine, 1, Wimpole Street, W.1, are open only to members.

The fourth international post-graduate course of the Tomarkin Foundation at Locarno will be held at Milan from September 12th to October 2nd, under the auspices of the Royal University of Milan. The course will include lectures on cancer, diseases of the heart, immunization against diphtheria, syphilis of the nervous system, disseminated sclerosis, poliomyelitis, and hormones. Further information can be obtained from the secretary, Tomarkin Foundation, Locarno, Switzerland.

We have received a preliminary programme of the eleventh annual session of the American Congress of Physical Therapy, to be opened on September 6th at the Hotel New Yorker, New York. The congress, which lasts for four days, is run on well-organized lines. There are sections comprising medicine, surgery, oto-laryngology, joints, colonic therapy, stomatology. An educational conference will take place on the first day. This will be "open" and will, in the words of the programme, "permit of an excellent opportunity for the physician and the technician to exchange ideas which will more directly further the relationship of doctor to assistant in the physical therapy specialty." Fifteen clinics will be available for inspection during the congress.

During the International Congress Against War, which is to be held at Amsterdam on August 27th and 28th, on the initiative of Romain Rolland and Henri Barbusse, an international medical congress will be held, of which the executive committee consists of the following members: Dr. Bönheim, director of the Hufeland Hospital, Berlin; Professor Biedl of Prague; Professor Kantorowicz of Bonn; Dr. Meng of Frankfort; Professor Pick of Königsberg, Dr. Simmel and Professor Zülzer of Berlin; and Professor Freud of Vienna. The following subjects will be discussed: (1) the effects of the world war on public health and the danger of a new world war; (2) the international collaboration of doctors to prevent war and the subsequent disasters in all countries; and (3) gas war.

The first international congress of Mediterranean hygiene will be held at Marseilles on September 20th, under the auspices of the medical faculty of that town, and under the patronage of the President of the Republic. The conference, which lasts for five days, will include discussions upon undulant fever, dengue, the de-ratization of ships, *spirochétose espagnole*, and *fièvre exanthématique Méditerranéenne*. An excursion to Provence has been arranged for September 25th. Special terms are offered in respect of boat and railway fares, and accommodation. The president of the congress is Professor E. Marchoux. For further information applicants are invited to communicate with Professor H. Violle (general secretary), Faculté de Médecine, Palais du Pharo, Marseille.

Mr. Henry Kimpton announces the publication, in September, of a new textbook of pathology by Professor William Boyd of the University of Manitoba. It consists of a royal octavo volume of about 950 pages, with 286 illustrations and a coloured plate—price 45s. net.

The German Orthopaedic Congress will be held at Mannheim from September 5th to 7th, when the following subjects will be discussed: fractures of neck of femur, introduced by Kreuz of Berlin and zur Verth of Hamburg; internal injuries to the knee-joint, introduced by Wittek of Graz; badly healed fractures, introduced by Böhler of Vienna, Hohmann of Frankfort, Bade of Hanover, and Blencke of Magdeburg; deformities of the thorax in kyphosis and scoliosis, introduced by Loeschke of Greifswald; plastic operations for dislocations of the hip, introduced by Schede of Leipzig and Spitzy of Vienna. Further information can be obtained from the president, Dr. Stoffel, Friedrich-Karlstrasse 3, Mannheim.

The committee responsible for the publication of the *History of the British Medical Association* has decided that the copies now available on the termination of the Centenary Meeting may be placed on sale. The price at which they are to be sold is 4s. 6d. postage paid. Orders should be sent, with remittance, to the Financial Secretary and Business Manager, B.M.A. House, Tavistock Sq., W.C.1.

Letters, Notes, and Answers

All communications in regard to editorial business should be addressed to **The EDITOR, British Medical Journal, British Medical Association House, Tavistock Square, W.C.1.**

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QUERIES AND ANSWERS

Sterilization of Dressings, etc.

ALLEN AND HANBURYS, Ltd., in reply to "K's" inquiry as to the time required for the sterilization of instruments and dressings in a Schimmelbusch sterilizer, write: This somewhat depends upon which sterilizer he has. The original Schimmelbusch sterilizer was constructed to blow off as soon as steam was generated. Although it is still being manufactured we discontinued making it some time ago, and now supply an improved type constructed to sterilize at a steam pressure of 10 lb. to the square inch. With this sterilizer it is recommended that the dressings should be subjected to 10 lb. pressure for twenty minutes, and afterwards left in the hot sterilizer to dry. With the original Schimmelbusch sterilizer it was recommended that dressings should be sterilized for thirty minutes, and afterwards left to dry. Owing, however, to the moist steam to which they were subjected, the dressings became very wet and it was almost impossible to dry them.

Income Tax

Basis of Assessment—Assistant

"T. M." did locum work from April, 1931, to September; from October to April, 1932, he was an assistant at £300 per annum, living in; in May, 1932, he became a partner. What is the basis of his liability?

*** He is not liable to account for tax on the value of his board and lodging, but only on the monetary remuneration provided by the agreement for service. (This does not prevent the employer from deducting the cost of the board and lodging as a professional expense.) Payments towards the purchase of the share in the practice are capital outlay, and cannot be deducted for income tax purposes.

LETTERS, NOTES, ETC.

Hyperpyrexia in Rheumatism

Dr. MAURICE C. BARBER (Bristol) writes: A few notes of a case of hyperpyrexia following rheumatic fever seem worth recording. On July 21st Mrs. W., aged 36, had synovitis of the right knee and a temperature of 102° F. Next day the left knee and right elbow were swollen and painful. Other joints were affected, but she was never very ill, though she had very profuse sweats. On August 5th she was much better, and the sweating ceased. On August 6th, when I was sent for, she had just started a convulsion and was unconscious. I took her temperature in the axilla—the mercury went to the top of the thermometer. Thinking there must be some mistake I took it again, with the same result. The thermometer is marked to 109°, so counting the space above as 1.5°, that gave a temperature of 110.5° at least—possibly higher. She was having convulsive movements of the head and limbs, the head movements being very violent. The pupils were contracted, and she had no corneal reflex; both eyeballs were drawn upwards. At 11.30 a.m. I started applying cold-water packs to the chest and abdomen and limbs. By 12.30 p.m. the temperature had dropped to 109°. At 1.30 p.m. it was 107°. The packs were continued, ice being obtained soon after starting them. By 6 p.m. the temperature was 105°. I drew off a catheter specimen of urine. There was no albumin or sugar. Next day her temperature was 103°. The convulsions continued, and she was quite unconscious. As the convulsions were evidently wearing her out I gave her an injection of morphine 1/4 grain, atropine 1/120 grain. I repeated this next day, and after this the convulsions practically ceased. On August 8th she was semi-conscious, and with difficulty swallowed some glucose water and milk. There was no sign of optic neuritis, and nothing abnormal in the fundi. There was no cardiac murmur, and nothing to be heard in the lungs. On August 11th she said she had no pain. Her condition remained much the same until August 13th, when she could not swallow, and was almost completely insensible again. On August 14th her breathing became very rapid and slightly stertorous, and she died at 6 p.m. The hyperpyrexia started sixteen days after I first saw her for the rheumatic condition. She lived for ten days after having a temperature of at least 110.5°. From the literature on the subject it is very unusual for a patient to live so long after such a high temperature.

A Link with the Eighteenth Century

The superintendent of Guy's Hospital has received a cheque for £100 from a correspondent whose father was born 125 years ago, while his father—the grandfather of the correspondent—was resident apothecary and medical officer of the hospital. The minutes of the meeting of the Court show that Richard Stocker, grandfather of the donor, was appointed apothecary on July 8th, 1795, and lived in the hospital, acting as apothecary and medical officer until October 16th, 1834, when he died and was succeeded in the post by a son—the uncle of the donor—who retired only a short time before his death in December, 1878. Thus two members of the Stocker family served the hospital over a period of eighty-three years. Many references to their work and their devotion to the hospital are to be found in the minutes of the Court, which are complete since the foundation of the hospital in 1725. It was made a condition of the appointment of the younger Stocker, James, that he must not practise outside the hospital, and must sleep inside it unless special permission were granted by the Treasurer. Richard Stocker is buried in the crypt of the hospital chapel, and lies near Thomas Guy, the founder.

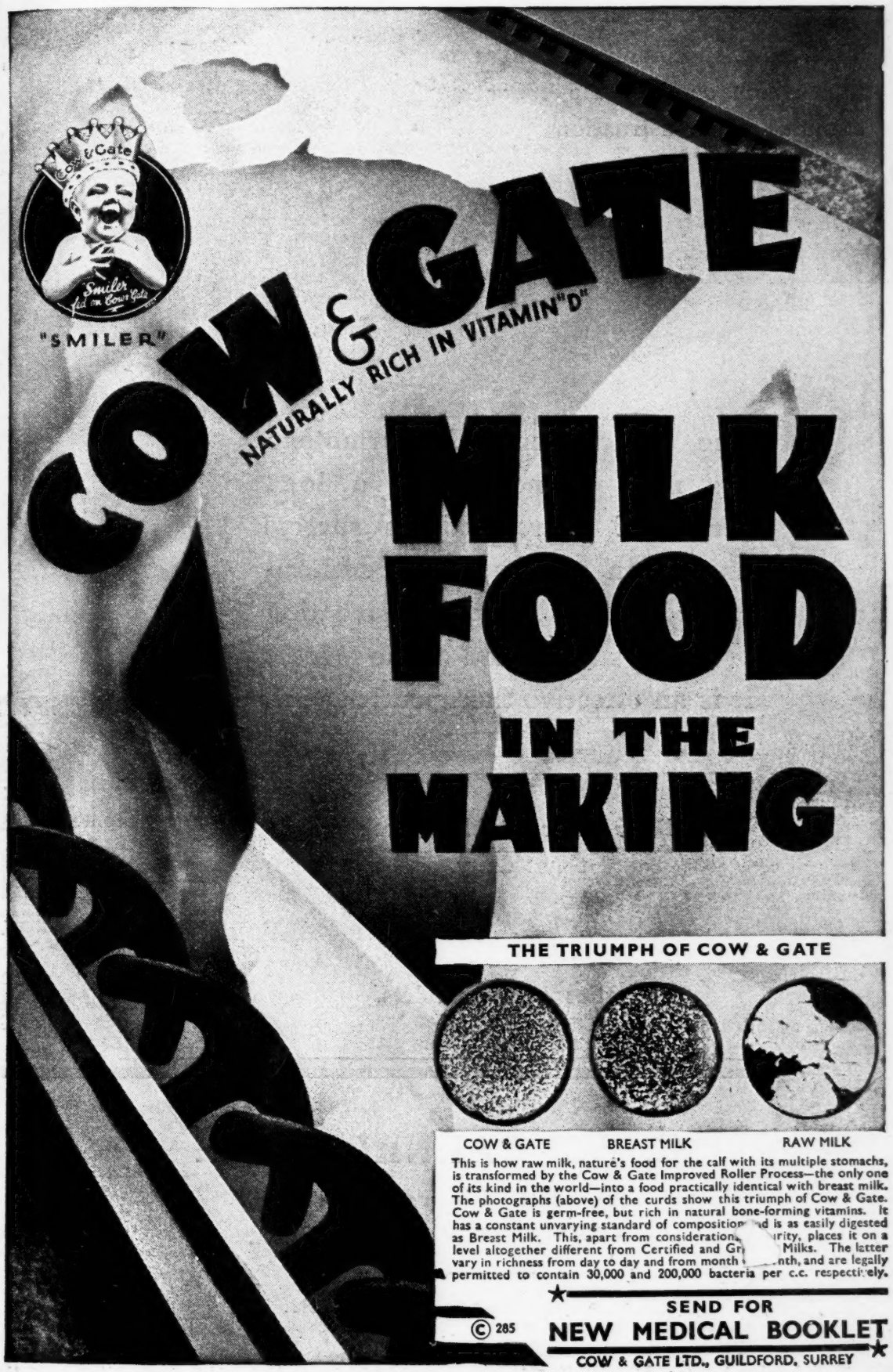
Correction

Major-General M. W. RUSSELL, late R.A.M.C. (Upper Walmer), writes: In the abstract (*Journal*, August 20th, p. 375) of the paper on British tropical medicine read for Dr. Philip Manson-Bahr in the Section of History of Medicine at the Annual Meeting, it is stated: "The names of Sir David Bruce and Sir William Leishman would for ever illuminate the records of the Indian Medical Service." This is an evident slip, for Sir David Bruce and Sir William Leishman both belonged to the Royal Army Medical Corps.

Vacancies

Notifications of offices vacant in universities, medical colleges, and of vacant resident and other appointments at hospitals, will be found at pages 30, 31, 32, 33, 35, 36, and 37 of our advertisement columns, and advertisements as to partnerships, assistantships, and locumtenencies at pages 34 and 35.

A short summary of vacant posts notified in the advertisement columns appears in the *Supplement* at page *168*.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